EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	7	homoallyl adj amine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L2	105294	ozone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L3	302	homoallyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L4	33	L2 and L3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L5	5	L2 same L3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L6	2	("20030097005").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L7	4	("2003097005").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L8	7	("2200788").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L9	23	"2200788"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L10	2	("6794542").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L11	8	("9802410").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19

EAST Search History

L12	0	("aminoadjacid").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:19
L13	341842	amino adj acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L14	5110	L2 and L13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L15	299	L2 same L13	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L16	581729	beta	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L17	579380	amine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L18	21	L15 same L16	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L19	304137	acetic adj acid	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L20	267	L2 near5 L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L21	0	L3 same L20	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L22	0	L13 same L20	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L23	1514	L2 same L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19

EAST Search History

L24	394	L2 near10 L19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L25	17	L20 same L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L26	5	"1351737"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L27	14	L20 near5 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L28	0	L20 near1 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:19
L29	15	L20 near10 L17	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:23
L30	348	(560/40).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:30
L31	657	(546/335).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:32
L32	608	(562/553).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/06/14 12:32
L33	1599	l30 or l31 or l32	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:33
L34	0	l3 and l33	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/06/14 12:33

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PASSWORD:
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NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
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NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
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NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
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NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
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NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
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NEWS 26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 28	MAY 01	New CAS web site launched
NEWS 29	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 30	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 31	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 32	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 33	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 34	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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```
=> homoallyl amine
           945 HOMOALLYL
        279198 AMINE
        258623 AMINES
        424834 AMINE
                 (AMINE OR AMINES)
L1          43 HOMOALLYL AMINE
                 (HOMOALLYL(W)AMINE)

=> ozon?
L2      107785 OZON?

=> l1 and l2
L3           0 L1 AND L2

=> amino acid
       1121857 AMINO
            44 AMINOS
       1121875 AMINO
                 (AMINO OR AMINOS)
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```
       4385732 ACID
       1577794 ACIDS
       4884863 ACID
                 (ACID OR ACIDS)
L4      714963 AMINO ACID
                 (AMINO(W)ACID)

=> l2(l)l4
L5         433 L2(L)L4

=> beta
       1459085 BETA
          1325 BETAS
L6     1459162 BETA
                 (BETA OR BETAS)

=> l5and l6
MISSING OPERATOR L5AND L6
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> l5 and l6
L7           82 L5 AND L6

=> d l7 72-82 ti

L7   ANSWER 72 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Structure of gentianine

L7   ANSWER 73 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Protein problems. VII. 5-Glutamal, 4-aspartal, and derived peptides

L7   ANSWER 74 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Stereochemical structures of kainic acid and its isomers

L7   ANSWER 75 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Condensation of phthalidylideneacetic acid with amino acids

L7   ANSWER 76 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Oxazoles and oxazolones

L7   ANSWER 77 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   The preparation of aldehydo compounds

L7   ANSWER 78 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   β -Acetamido-β ,.beta
     .-dicarbalkoxypropionaldehydes

L7   ANSWER 79 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Unsaturated amino acids. II. Allylglycine, .beta
     .-methallylglycine, and crotylglycine

L7   ANSWER 80 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   β -(Hydroxyphenyl)ethylamines and their transformations.
     III. Synthesis of benzylisoquinolines under physiological conditions

L7   ANSWER 81 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Constitution of cytisine

L7   ANSWER 82 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Action of ozone on hydrogenated and non-hydrogenated bases of the morphine
     series
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=> d l7 79 ti fbib abs

L7   ANSWER 79 OF 82  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Unsaturated amino acids. II. Allylglycine, .beta
     .-methallylglycine, and crotylglycine
AN   1949:2517  CAPLUS
DN   43:2517
OREF 43:574a-e
TI   Unsaturated amino acids. II. Allylglycine, .beta
     .-methallylglycine, and crotylglycine
AU   Goering, Harlan L.; Cristol, Stanley J.; Dittmer, Karl
SO   Journal of the American Chemical Society (1948), 70, 3310-13
     CODEN: JACSAT; ISSN: 0002-7863
DT   Journal
LA   Unavailable
GI   For diagram(s), see printed CA Issue.
AB   cf. C.A. 42, 8262c.  CH2:CHCH2(AcNH)C(CO2Et)2, refluxed 8 h. with concentrated
     HCl, gives 26% MeCH.CH2.CH(NH2).CO.O.HCl (I) and 34% CH2:CHCH2CH(NH2)CO2H
     (II), m. 255-8° (decomposition; m.ps. corrected) (Fillman and Albertson, C.A.
     42, 2930f, gave 212-15°).  II, refluxed 5.5 h. with concentrated HCl,
     gives 28% I and 32% II.  II in an equivalent of 0.1 N HCl, evaporated at room
     temperature in an air stream, gives the HCl salt, m. 164-8° (decomposition).
     Reduction of II gives PrCH(NH2)CO2H.  The free lactone from I yields
     3,6-diketo-2,5-bis(2-hydroxypropyl)piperazine (III), m. 173-4°
     [Fischer and Leuchs, Ber. 35, 3787(1902) gave 223-5°].
     CH2:CMeCH2(AcNH)C(CO2Et)2, refluxed 8 h. with concentrated HCl, gives 93% of
the
     γ-Me derivative (IV) of I, m. 210-11°.  CH2:CMeCH2CH(NH2)CO2H in
     1 equivalent N HCl gives IV.  IV and 2 N NaOH give γ-hydroxyleucine.
     AcNHCH(CO2Et)2 and MeCH:CHCH2Cl give 80% Et crotylacetamidomalonate (V),
     m. 47-8°; reduction in EtOH over Raney Ni at room temperature/30 lb. gives
     Bu(AcNH)C(CO2Et)2, m. 41-2° (Albertson, C.A. 40, 2796.7, reported
     it as an oil).  Et crotylacetamidocyanoacetate (VI), m. 56.5°, 76%;
     basic hydrolysis of VI gives 50% (V gives 30%) crotylglycine, decompose
     about 260°; 2-Bz derivative, m. 139° (Karrer and Itschner, C.A.
     29, 6210.6, gave 157°).  The structure of the amino
     acids was established by reduction to known compds. and by
     ozonolysis.


=> acetic acid
        244039 ACETIC
            22 ACETICS
        244048 ACETIC
                 (ACETIC OR ACETICS)
       4385732 ACID
       1577794 ACIDS
       4884863 ACID
                 (ACID OR ACIDS)
L8      214408 ACETIC ACID
                 (ACETIC(W)ACID)

=> l7 and l8
L9            5 L7 AND L8

=> d l9 1-5 ti

L9   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Chemistry and structure of ganefromycin

L9   ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Securinine and allosecurinine
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L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Total synthesis of strychnine

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Oxazoles and oxazolones

=> d l9 1-5 ti fbib abs

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemistry and structure of ganefromycin
AN 1994:107570 CAPLUS
DN 120:107570
TI Chemistry and structure of ganefromycin
AU Carter, Guy T.; Phillipson, Douglas W.; West, Robert R.; Borders, Donald B.
CS Lederle Lab., Am. Cyanamid Co., Pearl River, NY, 10965, USA
SO Journal of Organic Chemistry (1993), 58(24), 6588-95
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
AB Ganefromycins are antibiotics produced by Streptomyces lydicus sp. tanzanius having com. potential as performance enhancement agents for livestock. Ganefromycins are related to the elfamycin family of antibiotics but contain several unique chemical features which are the source of novel and unexpected chemical Reactions under mildly basic conditions resulted in the interconversion of α- and .beta .-ganefromycin by a 1,2-acyl migration. Strong base causes elimination of a trisaccharide whose structure was solved by single crystal x-ray diffraction anal. of the triacetate of the reduced ring-opened triol. Ammonolysis yields the same rearranged product from either α- and .beta.-ganefromycin. Evidence is provided for the mechanism of this rearrangement involving elimination of the saccharide to form a transient α, β -unsatd. carbonyl, Michael addition of ammonia, and intramol. transacylation. Ozonolysis and acidic methanolysis were employed to obtain simplified compds. for structure determination Ganefromycin β fragments in warm acetic acid solution, releasing the long-chain amino acid . 13C NMR data with assignments are provided for the degradation products.

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Securinine and allosecurinine
AN 1963:403684 CAPLUS
DN 59:3684
OREF 59:687f-h,688a-e
TI Securinine and allosecurinine
AU Satoda, I.; Murayama, M.; Tsuji, J.; Yoshii, E.
CS Nippon Shinyaku Co., Kyoto, Japan
SO Tetrahedron Letters (1962) 1199-1206
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB The previously isolated securinine (I), C13H15NO2 m. 141-2°, [α]25D -1089° (alkaline), pka' 7.17, was isolated from Japanese Securinega suffruticosa and a structure proposed on the basis of phys. and chemical data. IR absorption bands at 1792, 1764 cm.-1 (CCl4) and a broad UV spectral band at 256 mμ (ε 18,200) indicated the presence of an

α, β ; γ,δ-unsatd. γ-lactone,
recovered on acidification after alkaline hydrolysis. I hydrogenated by
Pd-SrCO3 in C6H6 or reduced with NaBH4 in alc. gave a dihydro derivative, an
α, β -unsatd. γ-lactone (II), C13H17NO2, m.
53.5°, [α]27D 5.9°, ν 1810, 1767 cm.-1 (CCl4),
λ 215 mμ (ε 17,700), pka' 8.35. I hydrogenated in alc.
with Pd-C or prereduced PtO2 gave a tetrahydro derivative, the γ-lactone
(III), C13H19NO2, m. 67-9°, pka' 9.03, ν 1789 cm-1 (CCl4),
λ 210 mμ (ε 1760), λ 210 mμ (ε 140,
HCl), indicating satn of III and the tetracyclic nature of I. II reduced
with LiAlH4 gave an oily diol (IV), C13H21NO2; HCl salt m. 165°,
ν 3226 cm.-1 (KBr). The salt in AcOH ozonized gave HOCH2CHO
and an oily α-ketol (V), C11H17NO2; HCl salt m. 213°, ν
3300, 1728 cm.-1 (Nujol). V reduced Tollens reagent but did not react
with Cu(OAc)2 in hot AcOH or with CrO3 in AcOH at 20°. V oxidized
with HIO4 gave an unidentified oxo-amino acid and gave
a monoxime, m. 207-8°, under forced conditions. V hydrolyzed with
tert-BuOK gave II indicating the impossibility of migration of the
exocyclic double bond to an enol lactone. The tertiary nature of the OH
group in V was indicated. I showed no NH absorption band in the IR and
gave a MeI salt without change of the UV absorption maximum at 256 mμ,
indicating that the N in I is isolated but near to the conjugated double
bonds. The conjugated double bond system was supported by the NMR
spectrum (60 Mc. in CHCl3, Me4Si as internal reference). I treated with Zn in
alc. H2SO4 at 20° gave a lactam (VI), C13H15NO, m.
74-5°,[α]25D 13.9° (alc.), ν 1634 cm.-1 (KBr),
λ 265, 272 mμ (ε 450,420), oxidized exhaustively with
KMnO4 to give o-HO2CC6H4CO2H. The smooth aromatization of I to VI was
rationalized by a 2-step mechanism. VI oxidized with a limited amount of
KMnO4 gave a hydroxy lactam (VII), Cl12H13NO2, m. 182-3°, ν
3300, 1661 cm.-1, λ 253 mμ (ε 4460), hydrogenolyzed over
Pd-C to a dehydroxy lactam (VIII), C12H13NO, m. 78-80°, ν 1675
cm.-1, showing that the OH is benzylic. The possible structures of VI,
VII, and VIII were discussed. I. MeI aromatized by Zn in H2SO4 gave an
oily ester (IX), C16H23NO2; HClO4 salt m. 171-2°, ν 1724, 759
cm.-1 (KBr), λ 266, 272 mμ (ε 840, 739). Treatment with
Zn in AcOH gave an a,β -unsatd. γ-lactone; HClO4 salt
m. 197-9°, λ 215 mμ (ε 13,600), ν 1742, 1678
cm.-1 I hydrogenated with Pd-C or prereduced PtO2 and the product
chromatographed over Al2O3, eluted with (Me2CH)2O to give III, and further
eluted with C6H6 containing 2% MeOH gave a crystalline hexahydro derivative
(X),
C13H21NO2, m. 223 5°, ν 3279, 1603- cm. (KBr), [α]24.5546
47.6°. The hydroxy lactam treated with HClMeOH gave a
γ-lactone, reconverted into X by percolation through Al2O3. In
addition to I, it was possible to isolate another minor alkaloid,
allosecurinine (XI), C13H15,NO2, m. 136-8°, [α]26D
-1082° (alc.), ν 1818, 1754, 1631 cm.-1 (Nujol), λ 257
mμ (ε 15,400), pka' 6.91; oxalate m. 174-6°. XI reduced
with NaBH4 gave a dihydroallosecurinine (XII), m. 85-6°,
[α]26D 25.2° (CHCl3), ν 1818, 1739 cm.-1, λ 215
mμ (ε 19,500). XI hydrogenated in alc. over prereduced PtO2
and the product chromatographed over Al2O3 gave, in addition to XII, a
hexahydro derivative, C13H21NO2, m. 263°, [α]24.5D 44.7°
(CHCl3), ν 3311, 1613 cm.-1 No tetrahydro derivative was obtained under any
hydrogenation conditions. XI aromatized with Zn in alc. H2SO4 gave a
lactam, m. 69°, [α]24.5D -32.7° (alc.), with an IR
spectrum identical with that of VI. Oxidation of the lactam with KMnO4 gave
VII and it was therefore concluded that XI is a stereoisomer of I,
possibly differing at the B/C ring juncture.

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Total synthesis of strychnine

AN 1963:81712 CAPLUS
DN 58:81712
OREF 58:14022g-h,14023a-h,14024a-h,14025a-h,14026a-h,14027a-h,14028a-c
TI Total synthesis of strychnine
AU Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K.
CS Harvard Univ.
SO Tetrahedron (1963), 19, 247-88
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA Unavailable
OS CASREACT 58:81712
GI For diagram(s), see printed CA Issue.
AB cf. CA 49,9001h. For the synthesis of strychnine (I) the selected point of departure was 2-veratrylindole (II). Acetoveratrone (25 g.) and 16 ml. PhNHNH2 swirled with 110 g. polyphosphoric acid with warming on a steam bath (exothermic reaction controlled by cooling) and the mixture heated 10 min. on a steam bath, poured into ice-H2O and extracted into 250 ml. hot CHCl3, the organic layer washed with 100 ml. H2O and the dried extract concentrated, the CHCl3 replaced by MeOH and the crystalline product (54.4%, m. 185-9°) recrystd. twice from CH2Cl2-MeOH gave II, m. 190-2°. PhNH2 (50 ml.) heated (oil bath) with 15 g. ω-bromoacetoveratrone and the mixture refluxed 1 hr. (oil bath, 175°), cooled to 50° and poured into 500 ml. ice-H2O containing 50 ml. dilute HCl, the H2O-washed precipitate taken up in CHCl3 and the dried solution filtered through 50 g. Al2O3, the filtrate evaporated and the residue crystallized from EtOH-MeOH yielded 39.5% II. The 1st steps in the construction of ring V involved transformation of II into 2-veratryltryptamine (III). II (5.6 g.) in 35 ml. 6:1 dioxane-AcOH added to 6.3 g. 25% aqueous HNMe2 and 1.71 g. 37% aqueous HCHO in 15 ml. cold AcOH and the mixture kept 2 hrs. at 20°, diluted with 300 ml. H2O and the clear, filtered solution basified with ice-cold aqueous KOH, the precipitate washed thoroughly with H2O and dried 12 hrs. in vacuo at 60° yielded 92% 2-veratrylgramine, m. 122-4°; picrate, m. 182-3° (Me2CO-EtOH). The gramine (6.3 g.) taken up in 25 ml. boiling C6H6 and the filtered solution kept 2 hrs. at 0° with 20 g. MeI in 50 ml. C6H6, the precipitate washed with Et2O, and then refluxed gently (N atmospheric) with stirring in 70 ml. HCONMe2 containing 1.22 g. NaCN 1 hr. with evolution of NMe3, the clear, cooled, yellow solution poured into 350 ml. ice-H2O and the H2O-washed precipitate dried at 60° in vacuo yielded 97% 2-veratryl-3-cyanomethylindole, m. 237-8° (alc.). LiAlH4 (50 g.) in 1100 ml. absolute tetrahydrofuran (THF) stirred vigorously 1 hr. with 12 addns. of 10 g. cyano compound at 5 min. intervals, the mixture stirred under reflux 2 hrs., and the cooled suspension treated cautiously with 100 ml. saturated aqueous Na2SO4 followed by 1000 ml. CHC3 and anhydrous Na2SO4, the mixture filtered through Celite and evaporated in vacuo, the viscous residue triturated with 500 ml. Et2O and the light yellow crystals (104 g., m. 142-5°) twice recrystd. gave III, m. 146-8°; HCl salt, m. 270-80° (decomposition). Construction of rings V, III, and IV followed. OHCCO2Et (33.6 g., freshly prepared from the corresponding ethyhemiacetal) in 250 ml. C6H6 added portionwise (exothermic reaction) to 97 g. III in 500 ml. warm C6H6, the solution refluxed 5 hrs. under a Dean-Stark head with separation of 5 ml. H2O and kept 16 hrs. at 5°, swirled with 500 ml. Et2O, and the product isolated yielded 113.9 g. Schiff base (IV), m. 170-80° (C6H6), λ 224, 245, 308 mμ (ε 31,600, 16,400, 20,800, all detns. in alc.). IV (45 g.) and 45 g. p-MeC6H4SO2Cl in 225 ml. C5H5N kept 18 hrs. at 20° and diluted with 300 ml. H2O, the mixture cooled

(ice-H2O) 30 min. and the H2O and MeOH-washed product dried at 60° in vacuo gave 40.9 g. crystals, m. 143-5° recrystd. to give the indolenine (V), m. 145-6°, λ 234, 339 mμ (ε 23,600, 15,600). To set the stage for more considerable operations, two simple changes were effected. V (6 g.) in 70 ml. hot alc. slowly treated with 2.5 g. NaBH4 in 2.5 ml. H2O and 20 ml. alc. and the mixture heated gently 1 hr., the clear solution diluted with H2O to incipient crystallization, and cooled to 5° yielded 5.11 g. crystals, m. 172-8°, recrystd. from CHCl3-MeOH to give the corresponding indoline (VI), m. 180-1°, λ 233, 287, 300 mμ (ε 24,200, 4500, 3200); N-acetyl derivative (VII) m. 206° (CHCl3MeOH), λ 235, 256, 280 mμ (ε 26,800, 18,000, 8000). VII (1.16 g.) in 25 ml. AcOH containing 10 drops of H2O ozonized 22 min. with ozonized O containing 0.295 millimoles O3/min. and the mixture poured into H2O, the precipitate taken up in CHCl3 and the solution washed with aqueous K2CO3. evaporated, and the neutral residue crystallized from MeOH yielded 29% of the mueonic ester (VIII), m. 165° (184°), ultra-violet spectrum showing increasing absorption below 310 mμ with weak, ill-defined shoulder at 285 mμ and shallow maximum at 230 mμ (ε 24,100). VIII (800 mg.) refluxed 10 hrs. in 30 ml. 5% HCl in MeOH and the solution evaporated, the crystalline residue taken up in 22 ml. 10:1 MeOH-CHCl3 and concentrated to 10 ml., kept several hrs. at 5° and the crystalline product (510 mg., m. 181-2°) recrystd. from MeOH yielded the pyridone (IX), m. 187-8° (MeOH), showing a highly characteristic ultraviolet and infrared absorption. Treatment of the total crude neutral product (15.95 g.) from ozonolysis of VII gave an over-all yield of 30% IX. IX (250 mg.) refluxed (N atmospheric) in 4 ml. MeOH containing 25 mg. Na and the solution cooled gave 41% 3-carbomethoxy-6H-pyrido[3,2,1-jk]carbazole-6-one, m. 180-1°, giving a strikingly characteristic ultraviolet absorption. The changes leading to the collapse of ring V were discussed; the difficulty caused by the p-MeC6H4SO2 group was eliminated. IX (750 mg.) refluxed 3.5 hrs. with 250 mg. red P in 10 ml. 1:1 AcOH-47% aqueous HI and the filtered solution evaporated, the residue recovered repeatedly from AcOH and triturated with 5 ml. Me2CO, the HI salt (400 mg.) acetylated 1 hr. at 20° in 3.2 ml. C5H5N and 4 ml. Ac2O and the mixture kept 30 min. with 2 ml. H2O, evaporated in vacuo and the semicryst. material rinsed with Et2O, taken up in 8 ml. hot H2O, and treated with 8 drops concentrated HCl, cooled and the N-acetylpyridone diacid (308 mg., m. 275°) taken up in 20 ml. MeOH, treated with freshly prepared CH2N2 in Et2O to cessation of N evolution, kept 1 hr. at 5°, and excess CH2N2 destroyed with AcOH, the residue on evaporation taken up in EtOAc and diluted with Et2O and C6H12 yielded 84% colorless N-acetylpyridone di-Me ester (X), m. 181.0-2.5° (EtOAc-Et2O), exhibiting a typical N-phenylpyridone chromophore in the ultraviolet absorption spectrum. X (900 mg.) refluxed (N atmospheric) 20 min. in 20 ml. MeOH containing 1 g. Na and kept cold 16 hrs. yielded 87.5% Na salt (XI), taken up (100 mg.) in H2O and acidified with HCl, extracted with CHCl3 and the dried extract evaporated gave 80 mg. free enol ester (XII), readily soluble in aqueous NaHCO3 to give a bright yellow solution, showing a pos., blue FeCl3 reaction, and exhibiting an ultraviolet absorption spectrum differing markedly from those of the simple N-phenylpyridones. C5H5N (23 ml.) containing 3.7 g. p-MeC6H4SO2Cl kept 10 hrs. at 20° with 768 mg. XI and diluted with 10 ml. H2O, followed shortly by 80 ml. 5N HCl, extracted with CHCl3 and the residue on evaporation of the neutral, washed solution crystallized from Me2CO yielded

95% of the enol tolylsulfonate (XIII), m. 217° (Me_2CO), λ 234,312, 317, 350-80 mμ (ε 23,900, 13,800, 13,700, 3800). MeOH containing $PhCH_2SNa$ (12 ml., prepared from 122 mg. Na and 670 mg. $PhCH_2SH$ in 100 ml. absolute MeOH) heated with 230 mg. XIII and the clear solution kept at 20° (N atmospheric) 3 hrs., filtered, and the precipitate washed with cold MeOH gave the benzylthio ester (XIV), m. 256-7° ($CHCl_3$-MeOH) λ 207, 253, 312 mμ (ε 31,000, 13,000, 14,000). XIV (500 mg.) in 100 ml. alc. refluxed 3 hrs. with 3 ml. alc. Raney Ni slurry and filtered, the residue washed with 100, 50, 50, and 50 ml. hot alc., and the residue on evaporation (398 mg.) taken up in a min. of Me_2CO, diluted with Et_2O, and filtered yielded 84% unsatd. ester, recrystd. twice from Me_2CO-Et_2O to give a colorless sample, m. 234°, λ 232, 310, 365 mμ (ε 25,600, 12,100, 4150). The unsatd. ester (252 mg., m. 185-215°) in 75 ml. alc. hydrogenated 2 min. at 20° with 50 mg. 10% Pd-C and the filtered solution evaporated yielded 72.5% racemic cis Me ester (XV), m. 186° (Me_2CO-Et_2O), softening at 160° exhibiting a typical N-phenylpyridone chromophore. The mother liquors yielded, on long standing, a small amount (20 mg.) of highly crystalline trans ester, m. 212° (Me_2CO-Et_2O). XV (440 mg.) refluxed 1 hr. in 15 ml. 2:1 MeOH-H_2O containing 220 mg. KOH and the MeOH evaporated in vacuo, the residue diluted with H_2O, and the nonacidic material (16 mg.) extracted with $CHCl_3$, the alkaline layer acidified with dilute H_2SO_4, and extracted with $CHCl_3$ yielded 388 mg. acidic material, recrystd. from MeOH to yield 59% rhombs, m. 271° (rapid heating), recrystd. 3 times from $CHCl_3$-MeOH to give racemic trans acid (XVI), m. 284° (decomposition, slow heating), showing an infrared spectrum identical with the spectra of the corresponding synthetic resolved acid and the acid from the degradation of I. A further crop of 48 mg. XVI was obtained by methylation of the mother liquors with CH_2N_2 and hydrolysis. XVI (30 mg.) in MeOH treated with excess CH_2N_2 in Et_2O and the residue on evaporation recrystd. twice from Me_2CO gave 24 mg. trans Me ester (XVII), m. 212° (Me_2CO-Et_2O), infrared spectrum identical with the spectra of the corresponding synthetic resolved ester and the ester from the degradation of I. XVII was identical in every respect with the Me ester, m. 212°, isolated as a byproduct from hydrogenation of the unsatd. ester. XVI (249 mg.) heated gently with quinidine [231 mg., m. 263-4° ($CHCl_3$-MeOH)] in 4 ml. 1:1 $CHCl_3$-MeOH and the residue on evaporation crystallized from $CHCl_3$-Me_2CO gave 114 mg. quinidine salt dihydrate, m. 160-72°, taken up in 10 ml. 1:1 H_2O-10% aqueous K_2CO_3 and extracted with $CHCl_3$, the aqueous solution acidified and extracted with $CHCl_3$ to give 51 mg. 1-trans-N-acetyl acid (XVIII), m. 295-300° ($CHCl_3$-MeOH), identical with the acid obtained by degradation of I. The apparently simple task of forming ring VI actually presented considerable preliminary difficulty since the trans disposition of Nb and the CO_2H group in XVIII required prior inversion at C-14. XVIII (200 mg.) refluxed 1 hr. in 20 ml. 1:1 C_5H_5N-Ac_2O and the residue on evaporation taken up in 20 ml. $CHCl_3$, the solution shaken 5 min. with 10 ml. cold 10% aqueous K_2CO_3 and the $CHCl_3$ solution washed with 10 ml. H_2O, the dried solution evaporated and the residue chromatographed from 2.5 ml. C_6H_6 on 8 g. neutral Al_2O_3, the column eluted with C_6H_6 and the eluate (235 mg.) treated with CH_2Cl_2-Et_2O yielded 93 mg. product, recrystd. to give 27.5% enol acetate (XIX), m. 250-5°, recrystd. from MeOH-Et_2O to give an anal. sample, m. 260-3°, λ 240, 258,335, 347,362 mμ (ε 21,300, 13,200, 7100, 8400, 5800). XIX (130 mg.) refluxed vigorously 6 hrs. in 6 ml. 1:1:1 concentrated HCl-AcOH-H_2O and the residue on evaporation taken up in dilute H_2SO_4, made alkaline with concentrated NH_4OH, and extracted with $CHCl_3$ gave 100 mg. colorless oily Me ketone (XX), showing a typical N-phenylpyridone chromophore ultraviolet

absorption spectrum. XX (100 mg.) kept 15 hrs. at 20° with 72.5 mg. SeO_2 in 6 ml. absolute alc. and the mixture refluxed 1 hr. on a steam bath, treated with C and the filtered solution evaporated, the residue taken up in 10 ml. 1:1 C_6H_6-$CHCl_3$ and filtered through C, diluted with 10 ml. $CHCl_3$ and extracted twice with 5 ml. dilute H_2SO_4, washed successively with 10 ml. H_2O, 10 ml. aqueous $KHCO_3$, and 5 ml. H_2O, the solvents evaporated and the neutral green oil (50 mg., containing traces of Se) taken up in 5 ml. MeOH, shaken with deactivated Raney Ni and the filtered solution diluted to 25 ml. with H_2O, heated 5 min. on a steam bath and treated with C, filtered while still hot and the residue washed twice with 5 ml. boiling H_2O, the cooled filtrate extracted with $CHCl_3$ and the residue on evaporation (21 mg.) crystallized from MeOH gave 12.4% dehydrostrychninone methanolate (XXI), m. 172-4° (resolidifying and m. 254-8°), $[\alpha]_{24D}$ -521 ± 4° (c 1.05, $CHCl_3$), identical with material prepared by degradation of I. The facile enolization of XX was confirmed by reconversion to the enol acetate XIX, by formation of the methylthio derivative (XXII), and by the production of the degraded ketone (XXIII) by hydrolysis of XIX with NaOH-MeOH in the presence of atmospheric O. XX (100 mg.) refluxed (N atmospheric) 4 hrs. in 10 ml. 1:1 Ac_2O-C_5H_5N and the residue on evaporation taken up in $CHCl_3$, the residue on evaporation (143 mg.) chromatographed on 5 g. neutral Al_2O_3 and eluted with 40 ml. 3:1 C_6H_6-$CHCl_3$ gave 99 mg. yellow foam, crystallized from CH_2Cl_2-Et_2O to yield 16.6% XIX, m. 260-3°. XIX (100 mg.) heated 30 min. in an open vessel on a steam bath with 1 ml. 2N aqueous NaOH in 5 ml. MeOH and the solution diluted with 20 ml. H_2O, the MeOH evaporated in vacuo at 40° and the aqueous solution extracted successively with 20, 10, and 10 ml. $CHCl_3$, the combined extract evaporated and the semisolid residue (57 mg.) crystallized from MeOH yielded 28 mg. material, m. 234-6°, recrystd. twice from MeOH-Et_2O to give XXIII, m. 237°, λ 237, 294, 319, 332, 347 mμ (ε 17,800, 13,200, 9200, 10,300, 7200). XX (2.18 g.), 1.60 g. p-$MeC_6H_4SO_2SMe$, and 3.6 g. anhydrous KOAc refluxed (N atmospheric) 4 hrs. in AcOH and the solvent removed at 60° in vacuo, the dark green residue taken up in $CHCl_3$ and the solution washed twice with aqueous 2N Na_2CO_3, extracted 5 times with 10 ml. 2N H_2SO_4, the acid extract basified with NaOH and extracted with $CHCl_3$, the ketone (1.94 g.) isolated as HCl salt monohydrate and recrystd. from MeOH gave 1.236 g. colorless needles of XXII.HCl.H_2O, m. 187-8° (MeOH). XXII.HCl.H_2O (543 mg.) shaken 1 hr. with 15 ml. 2:1 C_5H_5N-Ac_2O and the solution kept 10 hrs. at 20°, the solvents evaporated in vacuo and the residual oil taken up in 25 ml. $CHCl_3$, washed successively with 10 ml. each dilute H_2SO_4, dilute NaOH, and H_2O, and the dried extract evaporated gave 476 mg. colorless foam, crystallized from C_6H_6-C_6H_{12} to give 393 mg. product, m. 221-3°, recrystd. from MeOH to yield the N-Ac derivative, m. 223°, giving a typical N-phenylpyridone chromophore ultraviolet absorption spectrum. The conversion of dehydrostrychninone to I was undertaken. Purified C_2H_2 passed as a gentle stream into 30 ml. liquid NH_3 and stirred magnetically with portionwise addition of 150 mg. Na with change of color of the mixture from deep blue to gray, the NH_3 evaporated and the mixture heated 30 min. at 70% the dry HC.tplbond.CNa stirred in 20 ml. freshly prepared absolute THF and stirred at 0° with addition of dehydrostrychninone (XXI, 220 mg., heated 30 min. at 180-90° in a high vacuum with change of color to bright yellow on loss of MeOH) in 10 ml. THF, the mixture stirred 1 hr. at 20° and diluted with 25 ml. $CHCl_3$ and 10 ml. N HCl, the washed (aqueous $KHCO_3$, H_2O) and dried organic layer evaporated and the yellow foam (172 mg.) diluted with MeOH yielded 53% carbinol, recrystd. 3 times from $CHCl_3$-MeOH to give the ethinyl carbinol (XXIV), m. 302-5°. XXIV (500 mg.) in 50 ml. MeOH hydrogenated 3 min. with

deactivated Lindlar catalyst with uptake of 35.3 ml. H and the filtered solution evaporated in vacuo gave 432 mg. vinyl carbinol, m. 244-5° (MeOH). LiAlH4 (200 mg.) in 40 ml. Et2O refluxed with magnetic stirring in a Soxhlet apparatus and each half-filled thimble treated with 1 ml. solution (260 mg. XXIV in 10 ml. 1:1 Et2O-THF), the completed addition mixture refluxed 1 hr. and diluted with 40 ml. CHCl3 at 0°, decomposed with 2 ml. MeOH and 6 ml. H2O, the organic layer separated and the hydroxide slurry washed 3 times with 20 ml. CHCl8, the combined CHCl8 exts. shaken with 30 ml. H2O and the dried extract evaporated, the green oily residue (257 mg.) taken up in 10 ml. CHCl3 and extracted 3 times with 10 ml. N H2SO4, the aqueous layer basified with NH4OH and extracted with CHCl3, the basic product (243 mg.) chromatographed on 7.5 g. neutral Al2O3 and eluted with 40 ml. 1:1 C6H6-CHCl3 gave 156 mg. carbinol (XXV), crystallized from HCl in MeOH to yield 30% crystals, m. 192-200°, recrystd. from MeOH containing a drop of H2O to give the hydrochloride dihydrate, C21H22N2O2.HCl.2H2O, m. 195-205° (decomposition). The HCl salt (195 mg.) heated 2.5 hrs. at 120° (oil bath) in a 10-cm. long, sealed, glass tube in 4 ml. 30% HBrAcOH and 20 mg. red P with 3 cm. immersion to permit reflux, the cooled mixture filtered, and the residue on evaporation refluxed 30 min. with 10 ml. N H2SO4, diluted with 10 ml. H2O and the mixture boiled 1 hr., the clear yellow solution clarified with 200 mg. C and filtered while still hot, the cooled filtrate extracted twice with CHCl3 and the aqueous layer basified with 3 ml. NH4OH, extracted 4 times with CHCl3 and the residue on evaporation chromatographed on 4 g. activated neutral Al2O3 and eluted with 4:1 and 1:1 C6H6-CHCl3, CHCl3, and 20:1 CHCl3-MeOH gave a combination of 72.5 mg. partially crystalline and crystalline (m. 202-9°) fractions, recrystd. from MeOH to give 18.5 mg. material, m. 206-11°, recrystd. 3 times to yield synthetic isostrychnine (XXVI), m. 229-30° (evacuated capillary tube), [α]25D 23 ± 4° (c 2.54, alc.), identical with natural material prepared according to Leuchs and Schulte (CA 37, 34397). The noncryst. material from the combined fractions and the XXVI mother liquors evaporated in vacuo and the residue (84 mg.) acetylated at 20° in 5 ml. Ac2O and 0.5 ml. C5H5N, the acetylated product (98 mg.) chromatographed on 3 g. neutral Al2O3 and eluted with 5:3 C6H6-CHCl3 gave 65 mg. oily XXVI acetate, λ 5.86μ. XXVI (7mg.) and the acetate (65mg.) kept 15 min. in a long, sealed, glass tube at 20° with 4 ml. 1.5% alc. KOH and the mixture heated 5 hrs. on a steam bath, the fluorescent mixture diluted with 20 ml. CHCl3 and washed twice with H2O, the residue on evaporation (70 mg.) chromatographed on 4 g. neutral Al2O3 and eluted with 4:1 C6H6-CHCl3, the crystalline product (9.5 mg.) taken up in 1 ml. dilute H2SO4 and freed from 1.5 mg. nonbasic material with CHCl3, the aqueous layer made alkaline with NH4OH and extracted with CHCl3, the extract evaporated and the colorless product (8 mg.) recrystd. 3 times from CHCl3-Et2O gave brilliant colorless cubes of I, m. 275-85°, identical with natural material by m.p. and infrared spectral detns. Following completion of the total synthesis of I, miscellaneous reactions starting from dehydrostrychninone were reported. XXI (1.016 g.) heated 2 hrs. to 200° in vacuo and the yellow ketone taken up in 100 ml. dry C6H6, 3 g. activated Zn, 0.5 ml. freshly distilled BrCH2CO2Me, and traces of iodine and HgCl2 added, and the mixture refluxed with vigorous stirring (N atmospheric), the mixture treated 5 times at 40 min. intervals with 2 g. Zn and twice at 90 min. intervals with 0.5 ml. BrCH2CO2Me, the mixture refluxed altogether 5 hrs. and the cooled mixture diluted with 20 ml. MeOH, the dear solution decanted at 0° into 100 ml. 2N AcOH and the residual Zn washed twice with 50 ml. CHCl3, the organic layer extracted with 100 ml. dilute aqueous NH4OH and 50 ml. H2O, and the aqueous layer washed with 30 ml. CHCl3, the combined CHCl3 evaporated and the red-yellow oil (1.365 g.) taken up in 10 ml. Me2CO and cooled to 0° gave 410 mg. crystals, recrystd. from Me2CO to give the hydroxy ester A (XXVII), m.

260-4°, λ 5.78 μ. The mother liquor residues (1.1 g.) chromatographed on 50 g. neutral Al2O3 and eluted with 1:1 C6H6-CHCl3 gave 540 mg. colorless oil, diluted with 5 ml. Me2CO to give 209 mg. XXVII (total yield 42.5%). The Me2CO solution concentrated and the product (70 mg.) recrystd. 4 times from C6H6-Et2O gave the stereoisomeric hydroxyester B (XXVIII), m. 242-4°, λ 5.83 μ. XXVII (115 mg.) refluxed 5 hrs. in 15 ml. Ac2O and the residue on evaporation chromatographed on 5 g. Al2O3, eluted with 1:1 C6H6-CHCl3, and the pale, yellow, oily product crystallized from C6H6-C6HC12 gave 101 mg. acetoxy ester, m. 198-203°, λ 5.77, 5.79 μ (poorly resolved doublet). The acetoxy ester (59 mg.) pyrolyzed 12 hrs. at 200-50° in a high vacuum and the colorless sublimate recrystd. from MeOH gave 45 mg. α, β -unsatd. ester (XXIX), m. 244-8°, λ 5.82 μ. XXIX (42 mg.) in 10 ml. alc. hydrogenated with 10 mg. Pd-C with adsorption of 1 mole equivalent H and the filtered solution evaporated, the oily product chromatographed on 2 g. neutral Al2O3 and eluted with 1:1 C6H6-CHCl3 gave 43 mg. material, recrystd. from MeOH to yield 38 mg. colorless saturated ester (XXX), m. 265-8° (CHCl3-MeOH), λ 5.78, 5.98, 6.17, 6.27 μ (typical triplet N-phenylpyridone absorption). Reduction of XXIX or XXX with LiAlH4 in Et2O or THF gave very complex mixts. of products from which no pure compds. were isolated. A series of model redns. were recorded in connection with the reduction of the aromatic α-pyridone ring in XXI to the Δ12-dihydro-α-pyridone oxidation level, by addition of H at C-8 on the concave, more hindered side of the mol. Reduction of XXI by LiAlH4 in boiling Et2O gave the base in which the pyridone had been reduced precisely to the desired dehydro level. The structure was verified through the observation that the corresponding acetate (XXXI) was further reduced by LiAlH4 to a new base (XXXII), also produced by similar reduction of strychninclone b acetate (XXXIII; cf. CA 14, 1328). A proposed mechanism of reduction received confirmation from the interesting observation that strychninolone a acetate (XXXIV; cf. CA 8, 2718) is reduced under similar conditions. The base (300 mg., from XXXIV) in 15 ml. THF added slowly with stirring to 300 mg. LiAlH4 in 15 ml. THF and the mixture refluxed 4 hrs., cooled to 10° and diluted with 30 ml. CHCl3, swirled with 5 ml. H2O and decanted, the slurry washed with CHCl3 and the combined CHCl3 extracted 3 times with 10 ml. dilute H2SO4, the acid exts. made alkaline with NH4OH and extracted with CHCl3 gave 275 mg. basic reduction product, directly acetylated at 20° with 3.3 ml. 10:1 Ac2O-C5H5N and the basic acetate (235 mg.) chromatographed on 7 g. neutral Al2O3, eluted with C6H6, and the yellow material crystallized from MeOH-Et2O gave 102 mg. product, m. 190-3°, recrystd. from Me2CO-C6H12 to give dihydrostrychninol (XXXV) acetate, m. 193-4°, λ 254, 283, 292 mμ (ε 15,000, 4500, 3800), λ 6.00, 6.23, 5.79 μ. XXXIII (300 mg.) similarly reduced with LiAlH4 to a basic product (237 mg.) and crystal. from alc. gave the imino alc. XXXII, m. 240-3° (decomposition), λ 6.20, 6.74 μ, but no band in the 6 μ region. The mother liquors acetylated with 3.3 ml. 10:1 Ac2O-C5H5N followed by chromatographic purification on neutral Al2O3 gave 144 mg. imino acetate, m. 208-10° (MeOH-Et2O), λ 6.20, 6.75, 5.79 μ. XXI (190 mg.) in the thimble of a Soxhlet extracted into a boiling suspension of 200 mg. LiAlH4 in 30 ml. absolute Et2O 24 hrs. and the isolated basic material (156 mg.) chromatographed from CHCl3 on 4 g. activated neutral Al2O3, the eluate (106 mg.) acetylated and the crystalline acetate (97 mg., m. 215-18°) recrystd. from MeOH-Et2O gave strychninol b acetate XXXI, m. 217-19°, λ 254, 284, 294 mμ (ε 12,100, 4200, 3800), λ 6.0, 6.24, 6.75, 5.79 μ, also produced by reduction of dehydrostrychninolone (or its acetate) with LiAlH4. XXXI (63 mg.) extracted into a boiling suspension of 60 mg. LiAlH4 in 20 ml. absolute Et2O 4 hrs. and the isolated basic material (59 mg., m. 215-30°) recrystd. from MeOH gave 44 mg. pure XXXII, m. 237-40° (decomposition); acetate m. 206-9°. It was confirmed

that the racemic synthetic acid and its ester were identical with the corresponding optically active compds. obtained by degradation along essentially known lines but significantly modified with addition of new terminal stages. Oxidative degradation of I according to Leuchs and Schwaebel (CA 8, 694) yielded 23-4% strychninonic acid (XXXVI), m. 257-9°. XXXVI (44 g.) reduced with 245 g. 2.5% Na-Hg in 220 ml. at pH 7-8 (maintained by gradual addition of 2N HCl) and the clear solution made strongly alkaline with 80 ml. 10% aqueous NaOH gave 32 g. product, m. 208-13°, twice recrystd. from alc. to give strychninolone a, m. 228-31°. The ketone (20 g.) heated 2 hrs. on a steam bath in 110 ml. 10:1 Ac2O-C5H5N and the residue on evaporation taken up in 200 ml. CHCl3, washed successively with 20 ml. N HCl, 20 ml. saturated aqueous KHCO3, and 50 ml. H2O, and filtered through anhydrous Na2SO4 and the residue on evaporation crystallized from MeOH-Et2O yielded 88% product, m. 237-42°, twice recrystd. from alc. to almost colorless crystalline XXXIV, m. 242-4°. XXXIV (19.8 g.) in 300 ml. Ac2O at 115° streamed through vigorously with dry HCl and the solvent evaporated in vacuo, the residual oil taken up in 200 ml. CHCl3 and the solution washed with 100 ml. aqueous KHCO3 and 100 ml. H2O, the dried solution evaporated, and the residue crystallized from alc. yielded 85% XXXIII, m. 214-18° (with loss of EtOH at 135°). XXXIII (9.3 g.) and 17 g. Hg(OAc)2 refluxed 2 hrs. in 900 ml. AcOH and the solution decanted at 60°, streamed through 45 min. with H2S and filtered twice through Celite, the oily residue on evaporation taken up in 100 ml. CHCl3 and treated with 200 mg. C, the clear, filtered solution washed with 10 ml. dilute H2SO4, 20 ml. aqueous NaHCO3, and 30 ml. H2O, the residue on evaporation treated with C6H6-Et2O and the crystalline product (7.9 g., m. 268-78°) twice recrystd. from MeOH gave dehydrostrychninolone acetate, m. 282-5°, saponified (7 g.) with 800 ml. concd, aqueous NH4OH to yield 5.7 g. dehydrostrychninolone (XXXVII), m. 228-30°. CrO3 (5.7 g.) added cautiously to 50 ml. C5H5N (external cooling) and the red slurry treated with 5.7 g. XXXVII in 50 ml. C5H5N, the mixture kept 16 hrs. at 20° and poured into 500 ml. H2O, shaken vigorously with addition of 500 ml. CHCl3 and 3 g. Celite, filtered, and the aqueous layer extracted with CHCl3, the CHCl3 layer washed with 200 ml. H2O and the combined dried CHCl3 solns. evaporated in vacuo, the residue taken up in 100 ml. CHCl3 and washed with 40 ml. 0.5N H2SO4, 20 ml. 10% aqueous NaHCO3, and 40 ml. H2O, the residue on evaporation boiled in 125 ml. 4:1 C6H6-CHCl3 with C and Celite and the filtered solution concentrated to 25 ml., diluted with MeOH and heated briefly, the solution cooled and the combined crops (2.45 g., 1.55 g.) recrystd. from MeOH gave dehydrostrychninone methanolate XXI, m. 175-80° (loss of MeOH), solidifying to bright yellow crystals, m. 254-8°, infrared spectrum identical with that of synthetic material. Pulverized XXI (250 mg.) shaken 10-20 min. with 6.7 ml. aqueous 0.29N Ba(OH)2 and the clear yellow solution treated dropwise with 1.40 ml. aqueous 2.10% H2O2 in 10 min., the mixture stirred 3 hrs. at 20° and treated with 1.75 ml. N H2SO4, the stirring continued 15 min. and the solution filtered through Celite, the clear yellow solution (pH 9) extracted 3 times with 10 ml. CHCl3, the aqueous layer concentrated in vacuo at 50° to 2 ml. and diluted with 3 ml. Me2CO, slowly cooled and the product (115 mg., m. 300-5°) recrystd. from MeOH-H2O-Me2CO gave the trans amino acid, m. 305-8° (decomposition). The acid (200 g.) kept 16 hrs. at 20° with 5 ml. Ac2O and 2 ml. C5H5N and the residue on evaporation taken up in CHCl3 and extracted with dilute H2SO4 yielded52% trans-N-acetylamino acid, m. 295-300°, identical in all respects with the levorotatory XVIII. The acid (9 mg.) and 10 mg. quinidine taken up in CHCl3 and the residue on

evaporation recrystd. twice from MeOH-Me2CO gave 6 mg. colorless needles, m. 160-72°, undepressed on admixt. with the quinidine salt dihydrate isolated from XVIII. Esterification of the acid with CH2N2 in Et2O gave the Me ester, m. 196°, [α]22D -292 ± 5° (c 1.14, CHCl3), identical with XVII in the synthetic series. The acid (34 mg.) refluxed 4 hrs. in 2 ml. 5% HCl in MeOH and the residue on evaporation crystallized from MeOH-Et2O, the HCl salt (23 mg., m. 245-50°) taken up in 1 ml. C5H5N and heated 30 min. on a steam bath with 35 mg. p-MeC6H4SO2Cl, the mixture diluted with 0.3 ml. H2O and evaporated in vacuo, the residue taken up in 30 ml. 1:2 CHCl3-Et2O and washed with 5 ml. dilute H2SO4, 5 ml. 10% aqueous KHCO3, and 10 ml. H2O, the dried CHCl3-Et2O solution evaporated and the residue (26 mg.) recryst. from MeOH-Et2O gave 20 mg. trans-tolylsulfonylamino Me ester, m. 229°. Infrared measurements were used for control purposes through the investigation and 26 spectra, taken in CHCl3, of pure substances in the main line of synthesis were recorded.

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products
AN 1958:50699 CAPLUS
DN 52:50699
OREF 52:9163f-i,9164a-i,9165a-i,9166a-g
TI Constitution of conessine. X. Oxidation of conessine and pyrolysis of oxidation products
AU Haworth, R. D.; Michael, M.
CS Univ. Sheffield, UK
SO Journal of the Chemical Society (1957) 4973-83
CODEN: JCSOA9; ISSN: 0368-1769
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 51, 3641g. Oxidation of conessine (I) and its derivs. gave evidence favoring proposed structures for "α-oxyconessine" (II) and dioxyconessine (III). Oxidation and pyrolytic expts. similar to those used in the degradation of steroids gave I derivs. with a ruptured B ring, 5-membered B ring, and A and B rings degraded to a basic fragment which may be approached by synthesis. The nomenclature of the derivs. was based on the trivial name "conanine" for structure A with arbitrary α-configuration at position 5, on which basis I and III became 3. beta.-dimethylamino-5-conenine and 5,6-dihydroxy-3.beta .-dimethylaminoconanine, resp. Steroid nomenclature rules were applied and seco and nor prefixes used to indicate reductive bond rupture and ring contraction, resp., leading to the designation 5-oxo-5,8-seco-B-bisnorconanine for the parent structure (B). The system employed by Pinder and Robinson (C.A. 47, 1109g) was used for the nomenclature of the tricyclic ring. For products with unassigned configurations ordinary bond lines were used. Oxidation of I with SeO2 in hot H2O according to Bertho, et al. (C.A. 42, 2609b) gave 3β -dimethylamino-5-hydroxy-6-conenine (IV), m. 158°, ν 3382 cm.-1, acetylated according to Bertho (C.A. 45, 1608g) to the 5-AcO derivative (IVa), m. 128°, hydrolyzed with N KOH in MeOH to IV, stable to refluxing with Al(iso-PrO)3 or Al(tert-BuO)3 in PhMe-cyclohexanone. IV (250 mg.) in 20 ml. AcOH kept 87 hrs. with 90 mg. CrO3 in 1.5 ml. H2O and 4.5 ml. AcOH, the solution made alkaline with NaOH, extracted with Et2O, and the gummy product (230 mg.) crystallized from petr. ether and Me2CO gave an isomeric epoxide (V), C24H40N2O2, m. 163-4°. IV (100 mg.) and 0.15 ml. 30% H2O2 in 2.5 ml. 2N H2SO4 heated on a steam bath 3 hrs., the excess peroxide destroyed with SO2, the solution basified, extracted 3 times with Et2O, the extract evaporated, and the gummy peroxide (85 mg.) crystallized from Me2CO gave 21 mg. crystalline peroxide (Va), m.

225-6°. The Me2CO mother liquors evaporated, the residue taken up in ligroine, chromatographed on 2 g. Al2O3, eluted with 1:1 Et2O-ligroine, and the oily product crystallized from dilute Me2CO gave 28 mg. 3.beta .-dimethylamino-4,6-conadienine (VI), m. 116°, undepressed on admixt. with the product, m. 116°, of the action of POCl3 on IV (cf. Bertho, C.A. 46, 6129e), λ 2320, 2390, 2470 A. (log ε 4.3, 4.35, 4.2). Attempts to convert V and Va into triols were unsuccessful and oxidation of IV must be regarded as only provisional. I (500 mg.) in 10 ml. pure dioxane refluxed 3 hrs. with 780 mg. SeO2, the solvent evaporated, the residue diluted with H2O, the Se centrifuged off, the aqueous layer basified, extracted with Et2O, and the gummy product (180 mg.) chromatographed in C6H6 on 5 g. Al2O3 and eluted with C6H6 and CHCl3 gave 60 g. base, C24H40N2O2, m. 179-80° (C6H12) [picrate, m. 110° (Me2CO)], and 27 mg. base, C24H38N2O2, m. 240° (C6H6-ligroine). Similar results were obtained in C5H5N and in MeOCH2CH2OH. IVa (1 g.) and 1 g. OsO4 in 100 ml. dry Et2O kept 16 days at 20°, evaporated, the residue shaken overnight with 5 g. mannitol and 20 ml. N KOH, the alkaline solution extracted 3 times with Et2O, the combined exts. evaporated to 690 mg. residue, 303 mg. residue refluxed 1 hr. in 10 ml. N KOH in MeOH, evaporated, the residue taken up in H2O, extracted with Et2O, and the product chromatographed on 8 g. Al2O3 and eluted with Et2O and Et2O-CHCl3 gave 82 mg. IV and 110 mg. base, C24H40N2O2, m. 239-41° (C6H12). The above residue (276 mg.) heated 2 hrs. on a steam bath with 10 ml. H2SO4, basified, extracted with Et2O, and the product chromatographed on 8 g. Al2O3 gave 90 mg. VI and 38 mg. unidentified substance, m. 180° (C6H12). IVa (410 mg.) in 70 ml. Me2CO shaken with 420 mg. KMnO4 in 70 ml. Me2CO, evaporated, the residue taken up in Et2O, the solution washed with dilute aqueous NaOH, the dried extract evaporated, and the gum (337 mg.) chromatographed from Et2O-ligroine over 9 g. Al2O3 and eluted gave 210 mg. IVa and an oily base, C26H40N2O3, m. 128° [MeI derivative, m. 234-5° (Me2CO)], indicating that the basicity of 1 tertiary amino group had been destroyed either by oxidation of an N-Me to an N-CHO group, or by oxidation of an NCH2 group to an NCO group. Evidence in favor of the structure of (III) (dioxyconessine) was obtained by CrO3 oxidation of III, ν 3382, 3143 cm.-1, prepared according to Bertho (C.A. 42, 2609b) rather than by Warnecke's method [Arch Pharm. 226, 248(1888)]. III (200 mg.), 4 ml. C5H5N, and 1 ml. Ac2O heated 2 hrs. on a steam bath, the mixture evaporated in vacuo, and the residue diluted with 1 ml. H2O and kept 2 days over H2SO4 in vacuo gave 5,6-diacetoxy-3β -dimethylaminoconanine monoacetate (VII), m. 194-6° (decomposition) (Me2CO), converted by taking up in dilute HCl, basifying with dilute NaOH, filtering, and crystallizing the washed precipitate from dilute MeOH to the diacetylated base hydrate (VIIa), m. 130-5° (after resinification); MeI derivative, m. 296° (decomposition) (Me2CO). Attempted partial hydrolysis of VIIa was unsuccessful. III (565 mg.) in 40 ml. AcOH and 200 mg. CrO3 in 2.5 ml. H2O and 7.5 ml. AcOH kept 3 days at 20°, the excess CrO3 destroyed with 5 ml. MeOH, the basified solution extracted continuously 12 hrs. with CHCl3, and the extract evaporated gave 3β -dimethylamino-5-hydroxy-6-oxoconanine (VIII), m. 281-2° (alc.), subliming at 180°/10 mm., ν 3382, 1698 cm.-1, converted by refluxing 5 days with 98-100% HCO2H into an isomer, m. 193-5° (Me2CO), and a substance, m. 204-5° (decomposition) (Me2CO-ligroine). VIII gave no semicarbazone, Ac derivative, or enol acetate and was inert to SeO2, (CH2CO)2NBr, BzH, KIO4, and POCl3. Oxidative fission of ring B of III was effected with hot CrO3. III (11 g.) in 100 ml. 10% H2SO4 heated on a steam bath with slow addition of 5.5 g. CrO3 in 200 cc. H2O, the mixture kept 1 hr. at 100°, cooled, basified with Ba(OH)2, centrifuged, the residue washed with warm H2O, the combined washings and aqueous liquors boiled, the volatile bases passed into aqueous picric acid to give NHMe2 picrate, m. 157-8° (alc.), the

nonvolatile aqueous solution saturated with CO_2, filtered from precipitated $BaCO_3$, the filtrate evaporated in vacuo, and the residue (8.8 g.) crystallized from Me_2CO containing a small amount of H_2O gave 5-oxo-5,6-seco-3-conenin-6-oic acid (IX) sesquihydrate, $C_{22}H_{33}NO_3$-1.5H_2O, m. 193-6° (decomposition), λ 2270 A. (log ε 4.0), stable to heating 12 hrs. at 60°/0.01 mm. The insol. residue (6.5 g.) heated 6 hrs. with 150 ml. alc. HCl, and the gum (6.3 g.) chromatographed in ligroine on 120 g. Al_2O_3 and eluted with C_6H_6-ligroine and Et_2O yielded 3.3 g. Et 5-oxo-5,6-seco-3-conenin-6-oate (IXa), b0.03 195°, λ 2270 A. (log ε 4.0), and 120 mg. of an unidentified substance, m. 103-4° (ligroine). After rupture of ring B appropriate conditions for the addnl. removal of ring A following the elegant methods of Cornforth, et al. (C.A. 47, 11278i), were studied. IX (6.2 g.), 15 g. dry K_2CO_3, and 6 g. Fe filings heated with a free flame, the yellow distillate from 2 runs mixed with the Et_2O extract of the nonvolatile material, and the basic material extracted by washing the Et_2O extract with dilute HCl (leaving 380 mg. nonbasic material in the Et_2O), recovered by basification, isolated with Et_2O, chromatographed in C_6H_6-ligroine on 125 g. Al_2O_3, and eluted with C_6H_6-ligroine and C_6H_6 gave 2.20 g. oil, B-nor-3,5-conadiene (X), λ 2400, 2450 A. (log ε 4.1, 4.1), unreactive with maleic anhydride, and 190 mg. ketone (XI), m. 98-9° (dilute Me_2CO), sublimed at 80°/0.01 mm., ν 3436, 1738 cm.-1, giving a pos. Liebermann test [semicarbazone, m. 162-3° (dilute Me_2CO)]. A provisional structure, arising from the undetected aminotricarboxylic acid intermediate, was suggested for the ketonic base XI. X (196 mg.) in 10 ml. alc. hydrogenated at 20° with 390 mg. 5% Pd-C in 12 hrs. gave 180 mg. oily dihydro compound with no characteristic ultraviolet absorption maximum; MeI derivative, m. 257-8° (Me_2CO-Et_2O). III with hot CrO_3 and the amino acid mixture (15 g.) (containing IX) in 100 ml. alc. shaken 15 hrs. in H in the presence of 4 g. 10% Pd-C, filtered, and the solvent evaporated gave 5-oxo-5,6-secoconanin-6-oic acid (XII), no characteristic ultraviolet absorption spectrum in alc. XII (6.6 g.) and 3.3 g. dry K_2CO_3 heated, the residue distilled in vacuo, the distillate from 2 runs combined, and the basic fraction (6.2 g.) isolated as above, chromatographed in ligroine on 180 g. Al_2O_3, and eluted with ligroine and ligroine-Et_2O gave 3.37 g. colorless oil and 1.65 g. pale yellow oil. Crystallization of the former from Me_2CO gave B-nor-5-conenine (XIII), m. 78-9° and the Me_2CO mother liquors gradually deposited a dimorphous prismatic form, m. 78-9°. Inoculation of the latter oil with this form caused rapid solidification and in subsequent reactions the dimorphous forms were undistinguishable. XIII liberated iodine from HIO_3 but had no characteristic ultraviolet absorption spectrum; HCl salt, m. 268° (decomposition) (MeOH-Me_2CO); picrate, m. 100° (dilute Me_2CO); MeI derivative, m. 261-2° (Me_2CO-C_6H_6); dihydro derivative (prepared in AcOH with prereduced PtO_2), m. 67-8° (Me_2CO), not liberating iodine from HIO_3. XIII in Et_2O treated with 2N HCl, the crystalline HCl salt kept overnight in vacuo, the gummy product warmed 40 min. in dilute HCl on a steam bath, and the dried crystalline product recrystd. from Me_2CO-MeOH gave the isomeric HCl salt, m. 274° (decomposition), converted to the isomeric base B-nor-8(9)-conenine (XIIIa), m. 114.5-15°, stable to reduction with prereduced PtO_2 in AcOH, but readily liberating iodine from HIO_3. The behavior of XIII toward a number of oxidizing agents was examined HIO_3, H_2O_2 in acid solution, and CrO_3 gave intractable gums, and ozonolysis, followed by catalytic reduction of the ozonide, gave nonbasic amorphous material. Pyrolysis of the crude ozonolysis product resulted in the formation of 2-methy cyclohexanone and a noninvestigated higher-boiling nonbasic material unstable to light. XIII (128 mg.) and 1 g. KIO_4 in 40 ml. N H_2SO_4 kept 20 hrs. at 20°, cooled to 0°, basified with NaOH, and extracted with Et_2O gave 38 mg. 4,5,6-trihydroxy-B-norconanine, m. 234-5° (decomposition) (MeOH-Me_2CO). The mother liquors evaporated and the residue solidified under ligroine at 0° yielded 35

mg. 5,6-transdihydroxy-B-norconanine (XIV), m. 168-9 (C6H12). XIII (1 g.) and 1 g. OsO4 in 80 ml. Et2O refluxed 5 days, the precipitated osmic ester washed with Et2O, the filtrate and washings evaporated to give 333 mg. XIII, the precipitate shaken 12 hrs. with 5 g. mannitol in 30 ml. N KOH, the mixture diluted with 52 ml. H2O, extracted 4 times with CHCl3, the H2O-washed extract evaporated, the gum (650 mg.) chromatographed in Et2O on 20 g. Al2O3, eluted with Et2O, and the gummy product (450 mg.) triturated with ligroine gave 265 mg. 5,6-cis-dihydroxy-B-norconanine (XIVa), m. 184-5° (C6H12). XIVa (100 mg.) and 100 mg. KIO4 in 5 ml. N H2SO4 kept 40 hrs. at 20°, cooled to 0°, and basified with dilute NaOH gave 95 mg. 4,8-hydroxymethylene-5-oxo-5,8-seco-B-bisnorconanine (XV), m. 179-80° (C6H12), ν 1700, 3345 cm.-1; semicarbazone, m. 220-1° (Me2CO). In an attempt to induce a reversed aldolization the aldol base was treated with alkali. XV (50 mg.) in MeOH heated 90 min. (N atmospheric) with 160 mg. KOH in 1 ml. H2O, and the solution diluted with 5 ml. H2O, neutralized to pH 7 with 2N H2SO4, and filtered gave 29 mg. 5-hydroxy-5,6-seco-B-norconanin-6-oic 5,6-lactone, m. 131-2° (ligroine). XV (328 mg.) and 164 mg. K2CO3, pyrolyzed and the product treated as above, gave 42 mg. 2-methylcyclohexanone and 109 mg. basic fractions, purified by chromatography in ligroine over Al2O3 to 16 mg. unidentified oil; picrate, m. 226° (decomposition) (Me2CO). XV (100 mg.) and 31 mg. CrO3 in 9.5 ml. AcOH and 0.5 ml. H2O kept 50 hrs. at 20°, the excess CrO3 destroyed by addition of 5 ml. warm alc., the AcOH evaporated in vacuo, the residue basified with dilute NaOH solution, extracted with Et2O, and the product crystallized from dilute Me2CO gave 4,8-carbonyl-6-oxo-5,8-seco-B-bisnorconanine (XVI), m. 121-2°. XVI (100 mg.), 5 ml. saturated Ba(OH)2 solution, and 5 ml. H2O heated 2 hrs. on a steam bath, the mixture freed from unchanged XVI (3 mg.) with Et2O, the aqueous layer saturated with CO2, the mixture filtered, the filtrate evaporated, and the crude 5-oxo-5,6-seco-B-norconanin-6-oic acid (XVII) esterified with CH2N2 in Et2O gave the Me ester (XVIIa), m. 131-2° (ligroine); MeI derivative, m. 290° (decomposition) (Me2CO). XIVa (100 mg.) in 1 ml. 10% H2SO4 warmed 30 min. on a steam bath with 40 mg. CrO3 in 2 ml. H2O and the amino acid fraction isolated as above gave 52 mg. gum, methylated in Et2O with CH2N2 to XVIIa. XVIIa (50 mg.) heated at 335-40° in an evacuated sealed tube, and the product chromatographed in ligroine on 1 g. Al2O3 and eluted with Et2O-ligroine gave 25 mg. oily 5-hydroxy-5,6-seco-B-norcon-4-enin-6-oic 5,6-lactone; MeI derivative, m. 299-300° (decomposition) (MeOHMe2CO). XVII (200 mg.) and 100 mg. dry K2CO3 distilled over a free flame, the distillates from 4 runs separated into 160 mg. nonbasic (2-methylcyclohexanone) and 380 mg. basic fractions, and the basic material taken up in ligroine, filtered from 120 mg. insol. material, chromatographed over 9 g. Al2O3, and eluted with ligroine and ligroine-Et2O gave 50 mg. colorless oil and 132 mg. pale yellow oil with a powerful odor. The picrate of the colorless oil recrystd. 3 times from alc. gave 18 mg. de-AB-8-conenine picrate, m. 178-9° (decomposition); this treated with LiOH and the free base reduced with prereduced PtO2 in AcOH gave de-AB-conanine; picrate, m. 153-4° (dilute Me2CO). The picrate of the yellow oil twice recrystd. from Me2CO-CCl4 gave 9 mg. de-N-methyl-de-AB-8-conenine picrate, m. 236-8 (decomposition), decomposed with LiOH, and the de-N-methylde-AB-8-conenine extracted into Et2O. It had a very powerful odor and gave a pos. Liebermann nitroso test.

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TI Oxazoles and oxazolones
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TI Oxazoles and oxazolones
AU Cornforth, J. W.; Clarke, H. T.; et al.
CS Oxford Univ.;Princeton Univ. Press
SO Chemistry of Penicillin (1949) 688-848
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB OXAZOLE SECTION: New methods for constructing the oxazole ring have been devised and the behavior of functional groups elucidated. The synthesis of oxazoles and imidazoles from K β -hydroxy-α-(α-alkoxyalkylideneamino)acrylates is given. A mixture of 51.1 g. AmCN and 24.5 g. EtOH was kept with 19.2 g. dry HCl below 0° for 2 wk, decomposed with 74 g. K2 CO3 in Et2O and distilled The crude AmC(OEt):NH (62.4 g.), b11 52-65°, was shaken with cold aqueous H2NCH2CO2Et.HCl for 1 h. The upper layer was fractionated to yield Et α-ethoxycaprylideneaminoacetate (I),b0.5 91°, saponified on gentle warming to AmCO2Et. The corresponding Me α-methoxycaprylideneaminoacetate (Ia), b0.1 74°, was similarly prepared A solution of 0.85 g. K in 2.5 g. EtOH and 14 g. Et2O was diluted to 50 mL. with Et2O, cooled to -15° and treated with a similarly cooled mixture of 4.85 g. I and 3.2 g. HCO2Et, yielding after 3 h. at -10°, 2.6 g. of hygroscopic needles of C5H11C(OEt):NC(CO2Et):CHOK (II). The corresponding K Me β -hydroxy-α(α-methoxycaprylideneamino) acrylate (IIa) was obtained in 3.2 g.-yield from 3.75 g. Ia. Treatment of 2.6 g. II and 1.25 g. DL-penicillamine in 5 cc. EtOH with alc.-HCl gave crystalline DL-N-caproylpenicillamine, m. 137-8°. Treatment of II with ethereal HCl produced Et 2-amyl-oxazole-4-carboxylate, b0.07 99° (dinitrophenyl-hydrazone, m. 165-6°; amide, m. 152°) saponified to 2-amyl-oxazole-4-carboxylic acid, m. 92-3° (PhNH2 salt. m.98.5-9.5°) readily decarboxylated to 2-amyl-oxazole, b. 172-3°; picrate, m. 84.5-5.5°. This general synthesis of 2-substituted oxazoles and their 4-carboxylic acids has been extended to Et 2-phenyloxazole-4-carboxylate, m. 69-70°, the corresponding acid, m. 209°, and carried through to the known 2-phenyloxazole. The method can be also applied to the synthesis of imidazoles. Treatment of I with aqueous NH4OH gave 2-amylimidazole-4-carboxylic acid, m. 230° (decomposition); with MeNH2.HCl or alc. H2NCH2CO2Et.HCl, I produced, resp., Et 2-amyl-1-methylimidazole-4-carboxylate (III), m. 42-3°, and Et 2-amylimidazole-4-carboxylate-1-acetate (IIIa), m. 61°. Similarly, Ia gave Me 2-amyl-1-methylimidazole, m. 66.7°, and Me 2-amylimidazole-4-carboxylate-1-acetate, m. 107°. Hydrolysis of III and IIIa yielded 1-methyl-2-amylimidazole-4-carboxylic acid, m. 121-3°, and 2-amyl-4-carboxyimidazole-1-acetic acid, m. 132-4°. Starting from PhCH2CN, Et 2-benzylimidazole-4-carboxylate-1-acetate, m. 111-2°, was likewise prepared, converted by treating with MeOH into a Me Et ester. On heating with aqueous NH4OH and with PhNH2, 2-amyl-oxazole-4-carboxylic acid was converted into 2-amylimidazole, m. 33-4° and 1-phenyl-2-amylimidazole, m. 143-4°. Synthesis of oxazoles by rearrangement of oxazolones. The Na salt of 2-benzyl-4-hydroxymethylene-5-oxazolone (2.7 g.) in 50 mL. absolute MeOH was treated with 5 mL. absolute Et2O containing 0.38 g. HCl. The gummy product (2.28 g.) was taken up in 10 mL. absolute MeOH and heated for 30 min. with 6.2 mL. H2O containing 0.42 g. NaOH. The residue on evaporation was dissolved in 10 mL. of iced H2O, acidified with dilute HCl to pH 6.5 and extracted with Et2O, yielding 700 mg. 2-benzyloxazole-4-carboxylic acid, m. 158°. On heating at 220°, crude 2-phenyl-4-(α-hydroxyethylidene)-5-oxazolone rearranged to

2-phenyl-5-methyloxazole (IV), m. 184-5° (decomposition). Similarly, on heating to 230°, Na 4-hydroxymethylene-g-amyl-5-oxazolone rearranged to 2-amyl-oxazole-4-carboxylic acid. Evaporation of 2-(1-pentenyl)-4-(hydroxymethylene)-5-oxazolone in NaOH and fusion of the residue at 250° under reduced pressure yielded 2-pentenyl-oxazole-4-carboxylic acid, m. 145-7°. Incidental syntheses of oxazole derivs. The action of PhSO3Ag on Me thiobenzylpenaldate di-Et acetal produced colorless prisms of 2-benzyloxazole-4-carboxylic acid, m. 156-7° and the dehydration of Et α-benzylamino-acetoacetate gave Et 2-phenyl-5-methyloxazole-4-carboxylate, m. 51-2°, hydrolyzed to the acid, m. 180-1°, decarboxylated at 220° in the presence of a trace of CuO to IV. Thus a reaction known to succeed with α-acylamino ketones and carboxylic esters is extended to . beta.-keto esters. The 2-substituted oxazoles and their 4-carboxylic acids and esters are feebly basic, readily oxidized by cold aqueous KMnO4 but stable to Br in CCl4. The ring opens on warming with 2,4-(O2N)2-C6H3NHNH2 in 2N HCl with a tendency to formation of glyoxal osazone derivs. Rosenmund reduction of 2-amyl-oxazole-4-carboxylic acid chloride produced 2-amyl-oxazole-4-carboxaldehyde, b8 108° (2,4-dinitrophenylhydrazone, m. 172-3°), converted by warming with D-penicillamine-HCl in AcOH to the thiazolidine, devoid of antibiotic properties. From the corresponding Et ester, 2-benzyl-4-carboxyoxazole hydrazide, m. 81-3° and benzylamide, m. 121-2° were prepared In attempts to synthesize the thiazolidine-oxazolone structure for penicillin, attention was directed to the preparation of 5-alkoxyoxazoles and many variations of the general method of dehydrating α-acylamino esters with P2O5 were introduced. By the use of PCl5, P2O5, POCl3, SOCl2, and PhSO2Cl, the following new oxazoles were prepared (substituent given): 2-Ph, 5-MeO, b9 141°; 2-Ph, 5-PhCH2O, m. 56°; 2-PhCH2, 5-EtO, b15 152-4°; 2-PhCH2, 5-MeO, m.31-2°; 2-Am, 5-EtO, b0.8 82-5°; 2-Am, 5-MeO, b1.0 60-65°; 2-(1-C5H9), 5-EtO, b20 125-8° (C5H9 = pentenyl); 2-(1-C5H9), 5-MeO, b15 108-10°; 2-PhCH:CH, 5-EtO, m. 35°; 2-PhCH:CH, 5-Ph CH2O, picrate, m. 135° (decomposition); 2-Ph, 4-Me, 5-EtO, b10 151°; 2-Ph, 4-Me, 5-PhCH2O, picrate, m. 112-13°; 2-PhCH2, 4-Me, 5-EtO, b15 145-50°; 2-Am, 4-Me, 5-EtO, b3 92°; 2,4-Ph2, 5-EtO, m. 47-8°; 2-Ph, 4-PhCH2, 5-EtO, picrate, m. 105°; 2-Ph, 4-PhCH2, 5-PhCH2O, picrate, m. 117°; 2,4-(PhCH2)2, 5-EtO, b0.3 145-50°; 2-Am, 4-PhCH:CH, 5-EtO, m. 92°; 2-Ph, 4-CO2Et, 5-EtO, m. 75°; 2-Am, 4-CO2Et, 5-EtO, b0.1 122-5°; 2-(1-C5H9), 4-CO2Et, 5-EtO, b0.2 125°; 2-PhCH2, 4-CO2Et, 5-EtO, b0.1 165°. The possibility of converting an alkoxyoxazole to the corresponding oxazolone was realized by the catalytic hydrogenation of 2 g. of 2-phenyl-5-benzyloxyoxazole in 30 mL. dry dioxane in the presence of Pd-black to 2-phenyl-5-oxazolone, m. 91°. The converse reaction, transformation of an oxazolone to an alkoxyoxazole, has also been achieved. Methylation of 3 g. of 2-phenyl-4-carbethoxy-5-oxazolone with 500 mg. CH2N2 in 50 mL. Et2O yielded 2-phenyl-4-carbethoxy-5-methoxyoxazole, m. 72°. Similarly, methylation of 2-phenyl-4-carbomethoxy-2-oxazolin-5-one gave 2-phenyl-4-carbomethoxy-5-methoxyoxazole, m. 98°, identical with that prepared by the dehydration of BzNHCH(CO2Me)2 with PCl5 in CCl4. Attempts to obtain 5-alkoxyoxazole-4-carboxaldehydes covered a wide range. Formylation of BzNHCH2CO2Et and condensation with PhCH2NH2 in Et2O gave Et .beta .-benzylamino-α-benzamidoacrylate, R'NHCH:C(CO2Et)NHCOR (V; R = Ph, R' = PhCH2), m. 108°, cyclized by PBr3, POCl3 or PCl5 to 2-phenyl-4-benzylaminomethylene-5-oxazolone (VI), m. 134-7; Ac derivative, m. 140°. In the same way, Et β -benzylamino-α-phenylacetamido acrylate (VIa) with PBr3 gave 2-benzyl-4-benzylaminomethylene-5-oxazolone (VIb). Dehydration of Et α-benzamido- β ,β -diethoxypropionate with PCl5-POCl3 yielded 2-phenyl-4-(ethoxymethylene)5-oxazolone (VII). Distillation of benzyl α-benzamido- β ,.beta

.-diethoxypropionate gave a mixture of products including benzyl α-benzamido- β -ethoxyacrylate, m. 108-10°; benzyl 2-phenyloxazole-4-carboxylate, m. 106-7°; and VII. Attempts were made to cyclize α-benzyl- β -methyl-DL-phenylpenicilloate, HN.CH(CO2R').CMe2.S.CHCH(NHCOR)CO2CH2Ph (VIII, R = Ph, R' = Me) (VIIIa), m. 130°; dibenzyl-DL-phenylpenicilloate (VIII, R = Ph, R' = PhCH2) (VIIIb), m. 107-8°; and DL-2-(carboxy-1-hexenoylaminomethyl)-5,5-dimethyl-4-carbometh-oxythiazolidine benzyl ester (VIII, R = 1-pentenyl, R' = Me). (VIIIc). The action of PCl5 on VIII and VIIta gave definite evidence of formation of thiazolidinylalkoxyoxazoles and cyclization of VIIIb and chromatog. purification of the product gave benzyl 2-(2-phenyl-5-benzyloxy-4-oxazolyl)-5,5-dimethylthiazolidine-4-carboxylate, m. 120-5°, absorption band at 2850 A. This reduced in EtOAc using a Pd-BaSO4 catalyst with 2 mol H, corresponding to removal of 2 PhCH2 groups, yielded a product with no-antibiotic activity. The simpler thiazolidines were also investigated. The reaction of 3-methyl-2-(benzamidocarbethoxymethyl)-thiazolidine with PCl5 gave a Cl-containing product, converted by NaHCO3 to a probable sulfoxide. With PCl3, a product was obtained, which was converted by aqueous KOH to 2-phenyl-4-hydroxymethylene-5-oxazolone. β -Methylaminoethyl mercaptan-HI (from 15 g. of-2-methylthiazoline-MeI) in 20 mL. H2O was treated with 11 g. of crude Na salt of C,N-diformylglycine Et ester and neutralized with AcOH. After 15 h., NaHCO3 was added and the dried CHCl3 exts. (120 mL.) were concentrated to give 6.55 g. of crude product, converted by

treatment with 65.5 mL. of 10% HCl in EtOH to 4.4 g. of 2-(aminocarbethoxymethyl)-3-methylthiazolidine-2HCl (IX), m. 169-70° (decomposition). IX (10.0 g.) in 36.1 mL. of 2N NaOH and 35 mL. EtOH was stirred with 6.6 g. PhCH2CS2Me for 45 h., yielding 6.2 g. of colorless prisms of 2-[(phenylthioacetamido)carbethoxymethyl]-3-methylthiazolidine (X), m. 100-100.5°. Addition of 5.0 g X in 20 mL. CHCl3 to 8.6 g. PhSO3Ag and 2.5 mL. pyridine in 70-mL. CHCl3 gave no identifiable organic products. The action of PhSO3Ag on Me α-phenylthioacetamido- β ,.beta .-diethoxypropionate yielded a product from which Me-benzylpenaldate and 2-benzyloxazole-4-carboxylic acid were isolated. By the PCl5 method it has been possible to prepare 4-(2-thiazolyl)-2-benzyl-5-ethoxyoxazole and 2-(p-nitrophenyl)-4-(5,5-dimethyl-4-carbomethoxy-2-thiazolinyl)-5-ethoxyoxazole. Attempts to introduce a CHO group into the 4-position of 2-phenyl-5-ethoxyoxazole (XI) using PhNMeCHO and POCl3 gave 2-phenyl-4-anilinomethylene-5-oxazoline. With AcNHBr, XI gave 2-phenyl-4-bromo-5-ethoxyoxazole, b0.8 128°. The oxidation of 2-phenyl-4-methyl-5-ethoxyoxazole with SeO2, CrO3 or CrO2Cl2 resulted only in far-reaching breakdown. Condensation of PhCH2CH2COCO2H with AcNH2 or AmCONH2 gave α-acetamido- and α-caproyl-amino-γ-phenylisocrotonic acid (XII). Treatment of the Et ester of XII with PCl5 afforded 2-amyl-4-styryl-5-ethoxyoxazole (XIII), disrupted by ozonization with production of BzOH and H2NCOCO2Et. XIII (5.7 g.) in 100 mL. glacial AcOH was stirred with 9.0 g. of Pb(OAc)4 for 3 h., yielding 6.1 g. of 2-(1-acetoxyamyl)-4-styryl-5-ethoxyoxazole, m. 90-1°, degraded by distillation with loss of AcOH to 2-(1-pentenyl)-4-styryl-5-ethoxyoxazole (XIV), m. 100°, reduced catalytically to XIII. Oxidation of 2.83 g. XIV in 30 mL. tert-BuOH containing 0.75 g. H2O2 and 30 mg. OsO4 at 40-50° for 2 h. produced PrCHO and 5-ethoxy-4-styryl-oxazole-2-carboxaldehyde, m.130.5°, converted into the thiazolidine, m. 169°, using DL-penicillamine. Cyclization of AmCONHCH(CO2Et)2 in dry alc. free CHCl3 with PCl5, yielded 2-amyl-5-ethoxyoxazole-4-carboxylic acid (XIV), m. 63.4°, which on refluxing with PCl5 in CHCl3 gave Et 2-amyl-5-chlorooxazole-4-carboxylate (XV), b0.3 106°, catalytically reduced over Pd-BaSO4 in xylene to 2-amyl-oxazole-4-carboxylate, acidified to the free acid (XVa), m. 93-4°, converted by alc. EtONa to XIV. Treatment of 2 g. XVa with 1.09 g. PCl5 in 10 mL. CHCl3 and distillation produced the corresponding acid

chloride, b0.3 96°, converted by (NH4)2CO3 in aqueous NH4OH to the amide, m. 90°, which, distilled with P2O5, gave 2-amyl-5-chloro-4-cyanooxazole (XVb), b0.15 72°. Reduction of 3.0 g. XVb in a suspension of 5.7 g. anhydrous SnCl2 in 40 mL. dry ether yielded unstable 2-amyl-5-chloro-oxazole-4-carboxaldehyde (XVI) (dinitrophenylhydrazone, m. 109-10°), rearranging in 3 days at room temperature or on low pressure distillation to 2-amyl-oxazole-4-carboxylic acid chloride. Despite its instability, XVI readily combined with D-penicillamine-HCl to produce D-2-(2-amyl-5-chloro-4-oxazolyl)-5,5-dimethylthiazolidine-4-carbo-xylic acid-HCl, m. 150-2° (decomposition). A similar series of compds. starting with Et 2-phenyl-5-ethoxyoxazole-4-carboxylate (XVII) and proceeding to the thiazolidine was later prepared XVII was saponified to the crystalline acid (XVIIa), m. 148°, converted to the acid chloride (XVIIb), m. 105-6°, and to Et 2-phenyl-5-chlorooxazole-4-carboxylate, m. 68°, by refluxing in xylene for 1 h. The corresponding acid (XVIII), m. 178-4° (decomposition), was converted through the acid chloride, m. 118-20°, the amide, m. 183°, and the cyano compound, m. 112°, to 2-phenyl-5-chlorooxazole-4-carboxaldehyde (XIX), m. 91-3°. The addition of 1.14 g. aldehyde in 5 mL. EtOH and 10 mL. Et2O to 0.93 g. D-penicillamine-HCl in 5 mL. H2O and 0.65 g. AcONa, and passage of HCl through a filtered ethereal solution of the reaction product, yielded 1.5 g. of 2-(2-phenyl-5-chloro-4-oxazolyl)-5,5-di- methylthiazolidine-4-carboxylic acid-HCl, m. 178° (decomposition); Me ester-HCl, m. 120-2°; free acid, m. 166°; Me ester, m. 154°; PhCH2 ester, m. 116-7°. The thiazolidine exhibited a low order of antibiotic activity. A similar series of 2-benzyloxazole derivs. have been prepared but the corresponding thiazolidine was inactive: 2-benzyl-5-ethoxy-oxazole-4-carboxylic acid, m. 118° (decomposition); Et ester, b0.1 165°; acid chloride, m. 81-2°; 2-benzyl-5-chlorooxazole-4-carboxylic acid, m. 183° (decomposition); Et ester, b0.02 170-5°; acid chloride, m. 156-7°; cyano compound, m. 49-50°; aldehyde [dinitrophenylhydrazone, m. 173°; semicarbazone, m. 185° (decomposition)]; 2-(2-benzyl-5-chloro-4-oxazolyl)-5,5-dimethylthiazolidine-4-carbo-xylic acid-HCl, m. 176-7° (decomposition). By refluxing 223 mg. XVIII in 3 mL. EtOH with 40 mg. Na, the Cl was replaced by the EtO group with formation of the corresponding acid, XVIIa. Distillation of the aldehyde XIX at 0.1 mm. gave 2-phenyloxazole-4-carboxylic acid chloride, m. 107-8°, transformed by stirring with cold concentrated aqueous NH4OH to the amide. Similarly the acid chloride XVIIb was converted to the amide, m. 118-19°, rearranged by heating for a few rain. at 140° to Et 2-phenyl-5-aminooxazole-4-carboxylate, m. 183deg;. All oxazoles found to undergo rearrangement may be formulated as 5-substituted oxazoles having a CO group in the 4-position, the general case being N:CR'.O.CR3:CCOR2 → N:CR'.O.CR2:CCOR3. Known examples of rearrangement are tabulated. Since the mol. is unstable when R3 and R2 are Et and Cl, resp., or when R3 and R2 are Cl and H, resp., it is deduced that the ethoxy aldehydes should show too great stability for successful synthesis. Cyclization of AmCONHCHCNCO2Et with P2O5 in CHCl3 gave 2-amyl-4-cyano-5-ethoxyoxazole, b0.03 98°, not reduced to the aldehyde by SnCl2 in Et2O. No 4-acetyloxazole was obtained from the MeMgI reaction product but the isolation of Et α-caproylaminoacetoacetate (dinitrophenylhydrazone, m. 166-7°) indicated oxazole ring cleavage. The dehydration of 2-phenyl-5-ethoxyoxazole-4-carboxyamide with POCl3 or the ethylation with MeCHN2 of the crude oxazolone obtained by treating BzNHCHCNCO2H with Ac2O produced 2-phenyl-4-cyano-5-ethoxyoxazole, m. 77°. The previously unknown 5-aminooxazoles were prepared thus: treatment of 7 g. BzNHCH(CN)CO2Et, m. 138°, in 125 mL. CHCl3 with 6.2 g. PCl5 gave 4.5 g. Et 2-phenyl-5-aminooxazole-4-carboxylate, m. 185°, also prepared by the action of POCl3 on Bz-NHCH(CONH2)CO2Et. Condensation of 1.18 g. H2NCH-(CO2Et)2 with 1.13 g. PhNHOEt by heating for 30 min. at 110° gave the alternative compound, formulated as

2-phenyl-4-carbethoxy-5-imidazolone, m. 275°. Similarly were prepared Et 2-benzyl-5-aminooxazole-4-carboxylate (XX), m. 124° and the corresponding 2-benzyl-4-carbethoxy-5-imidazolone, m. 254° (decomposition); 2-(1-pentenyl)-4-carbethoxy-5-aminooxazole, m. 105°; 2-amyl-4-carbethoxy-5-aminooxazole (XXa), m. 104° and the corresponding 2-amyl-4-carbethoxy-5-imidazolone., m. 230° (decomposition). On heating at 170° for 5 min., XXa was entirely converted into AmCONHCH(CN.)CO2Et, m. 83°. Heating either XX or PhCH2CONHCH(CN)CO2Et at 160-70° for 15 min. produced an equilibrium mixture with the open chain ester predominating. This same mixture was formed by heating 2-benzyl-5-ethoxyoxazole-5-carboxylic amide, probably through initial rearrangement to the aminooxazole. Stirring 35 g. NCCH2CO2CH2Ph in 40 mL. of chilled glacial AcOH with saturated aqueous NaNO2 (16.5 g.) yielded 29 g. NCC(NOH)CO2CH2Ph, m. 119°, reduced with Al-Hg to NCC(NH2)CO2CH2Ph, m. 95°, and benzoylated to NCCH(NHBz)CO2CH2Ph, m. 130°, converted by heating at 160° for 5 min. to 2-phenyl-4-carbobenzyloxy-5-aminooxazole, m. 203°. The 4-carbethoxy-5-aminooxazoles are feebly basic substances whose HCl salts dissociate readily. XXa.HCl, on boiling with ethereal EtOH gave AmCONHCH(CONH2)CO2Et, m. 150-1°, along with NH4Cl. Treatment of 1 g. XXa in 10 mL. dry Et2O at -15° with NOCl gave a low yield of Et 2-amyl-oxazole-4-carboxylate, m. 92-3°. Formylation of 15 g. BzNHCH2CN in 200 mL. HCO2Et and 100 mL. benzene by addition of NaOEt (from 2.16 g. Na) in 100 mL. benzene produced, after treatment of the intermediate BzNHC(:CHONa)CO2H with dilute H2SO4 to pH 4, 2-phenyl-5-aminooxazole-4-carboxaldehyde (XXI), m. 172-3°, probably in the tautomeric form. Formylation of AmCONHCH2CN and distillation of the product yielded 2-amyl-oxazole-4-carboxylic acid amide, m. 154-5°, evidently by rearrangement of XXI. The action of POCl3 on Bz-NHCH(CONH2)2 and AmCONHCH(CONH2)2, m. 231°, gave 2-phenyl-5-amino-4-cyanooxazole, m. 233° (Ac derivative, m. 202-3°), and 2-amyl-5-amino-4-cyanooxazole, m. 117°. These aminooxazoles could not be reduced to aldehydes.

Saturation of 0.52 g. PhCH2CSNHCH(CN)CO2Et, m. 157°, treated in 5 mL. dry EtOH with dry HCl at -10° and the solution evaporated after 12 h. at 20° in vacuo yielded 0.5 g. 2-benzyl-4-carbethoxy-5-aminothiazole, m. 180°. OXAZOLONE SECTION. Part. I. General Chemical of Oxazolones. Preparation of 2-Oxazolin-5-ones. The reaction of Ac2O with α-acylamino acids is the most general procedure by which new oxazolones, O.CR:N.CR1R2.CO, have been prepared (substituents given): 2-Me, 4-iso-Pr, b10 60°; 2-PhCH2, 4-Me, b0.5-1.0 122-3°; 2-PhCH2, 4-iso-Pr, b0.5 115-17°; 2,4-(PhCH2)2, oil; 2-Am, 4-PhCH2, b5 135-8°; 2-(2-pentenyl), 4-PhCH2, b1.0 155-7°; 2-PhCH2, 4,4-Me2 (I), m. 59.5°; 2-Ph, 4-iso-Bu, m. 56-7°; 2-PhCH2, 4-sec-Bu, b2.0 137-9°; 2-Ph, 4,4-C5H10, m. 71°; 2-PhCH2, 4-Me, 4-PhCH:CH, m. 56-7°; 2-Ph, 4-CO2Et, m. 147-8°; 2-Am, 4-CO2Et, oil; 2-Ph, 4-(p-MeOC6H4CH2); 2-PhCH2, 4-(p-MeOC6H4CH2); and 2-PhCH2, 4-iso-Bu. Similarly, heating 100 g. BzNHCH2CO2H (II) in 300 mL. Ac2O at 100° yielded 49 g. 2-phenyl-2-oxazolin-5-one (III), m. 94-5°, the only monosubstituted oxazolone prepared by this method. By warming BzNHCHPhCH2CO2H in CHCl3 with 1 equivalent of 2-benzyl-4-methyl-5-oxazolone, a good yield of 2-phenyl-4-benzyl-5-oxazolone, m. 68-9°, was obtained. Addition of 1 g. NaNO2 in 20 mL. H2O to 3 g. of BzNHC(CONHNH2):-CHPh in 30 mL. N HCl gave α-benzamidocinnamic azide, m. 113-4° (decomposition), converted on boiling with EtOH or treatment with pyridine at room temperature to 2-phenyl-4-benzylidene-5-oxazolone (IV). Similarly, Me2C:C(NHBz)-CON3 was converted to 2-phenyl-4-isopropylidene-5-oxazolone (IVa). These type II (unsatd. substituent at the 4-position) unsatd. oxazolines are formed more readily than the above-listed type I (saturated substituent at the 4-position) saturated oxazolones to which the azide conversion could not be extended. Reduction of IV over Pd-C gave

2-phenyl-4-benzyl-5-oxazolone (V), m. 67-8°. IVa was similarly reduced in dioxane to give an oil which, treated with PhNH2 in benzene, produced Me2CHCH(NHBz)CONHPh, m. 211-2°. The possibility arose that any reagent capable of transforming an acid to its chloride might be expected to convert an α-acylamino acid to the corresponding oxazolone. Thus treatment of II in 15 mL. dioxane with 2 mL. PBr3 gave III. Similarly, 14.5 g. PhCH2CONHCMe2CO2H in 150 mL. dioxane was treated with 18 g. PBr3. The solid product suspended in dioxane and treated with slight excess of CH2N2 in ether yielded I, converted by PhCH2NH2 into PhCH2CONHCMe2CONH2, m. 122-3°. Treatment of PhCH2CHNHBzCO2H in pyridine with PBr3 likewise gave the known V. Attempts to prepare 2-benzyl-5-oxazolone from PhCH2CONHCH2CO2H gave an unstable oil, converted by PhCH2NH2 into PhCH2CONHCH2CONHCH2Ph. Conversion of PhCH:C(NHBz)CO2H into IV was effected by POCl3, SOCl2, pyridine, by ClCH2COCl and K2CO3, and by AcCl in dioxane. Oxazolones have been produced by treating PhCH2OCOCl with acylamino acids. Apart from direct dehydration, three methods are known for the preparation of type II oxazolones; the Erlenmeyer aldehydeacylglycine synthesis, the Bergmann-Stein reaction of N-(α-haloacyl) amino acids with Ac2O, and the dehydration of β -hydroxy-α-acylamino acids. In that III reacts with Me2CO in the presence of NaOAc to yield IVa in the absence of Ac2O, it is suggested that III is an intermediate in the Erlenmeyer synthesis. In the presence of a little pyridine, BzH condenses with III to produce IV. Similarly, 2-phenyl-4-propylidene-5-oxazolone, m. 88-9°, was obtained in good yield from III and EtCHO. By adding Ac2O dropwise with stirring to 17.9 g. II and 6.1 g. fused NaOAc in 580 mL. Me2CO, refluxing for 3-4 h. at 59-62°, pouring the reaction mixture over 200 g. ice and diluting to 1500 mL. produced high yields (73%) of relatively pure 2-phenyl-4-isopropylidene-5-oxazolone, m. 98°. Condensation of II with (EtO)2CHCHO and Ac2O gave 4,4'-glyoxalidenebis(2-phenyl-5-oxazolone), m. 325° (decomposition). Though no acyl interchange in the Erlenmeyer synthesis occurs with II, the formation of 2-methyl-4-benzylidene-5-oxazolone occurs when either PhCH2CONHCH2CO2H or AmCONHCH2CO2H (VI) is refluxed with BzH in the presence of Ac2O and NaOAc. Refluxing VI (15.1 g.) with 13.1 g. AmCO2Na and 61 g. (AmCO)2O in 49 mL. Me2CO for 24 h. at 75° gave α-caproyl-amino- .beta .,β -dimethylacrylic acid, m. 162-3°, converted by melting and heating in vacuo at 180-90° into 2-amyl-4-isopropylidene-5-oxazolone, b0.03 60-2°. By Bergmann's method, 2-methyl-4-isopropylidene-5-oxazolone (VII) and 2-methyl-4-sec-butylidene-5-oxazolone were prepared from Me2CHCH2CH(NHCOCH2Cl)CO2H and EtMeCHCH-(NHCOCH2Cl)CO2H. Carter's method was used to prepare VII by the action of Ac2O on Me2C(OMe)CHNH2CO2H. Ring opening Reactions of Oxazolones. The general reaction of oxazolones with H2O, ROH, RSH, NH3, RNH2 and RR'NH represented by O.CR:N.CR1R2.CO + HX → OCRHNCR1R2COX, suggested originally the thiazolidine-oxazolone formulation of penicillin. Comparison of the reactivity of V with that of IV showed the former to be rapidly hydrolyzed by 2N aqueous acid or alkali under conditions not affecting the latter. V reacts with ROH more rapidly than III. In the presence of NaOMe or PhCH2NMe3-OH, IVa was converted quant. to Me2C:C(BzNH)CO2Me, m. 130-1°. The methanolysis of 2-benzyl-4-p-methoxybenzyl-5-oxazolone in dry absolute MeOH yielded (N-phenylacetyl-p-methoxyphenylalanyl)-p-methoxyphenylalanine, m. 199-200°. The formation of the dipeptide may be due to an "ortho-ester" reaction with the imino-ether form of the oxazolone. Reaction of PhCH2SH with III and I yielded benzyl hippurate, m. 101-2° and Me2CHCH(NHCOCH2Ph)COSCH2Ph, m. 138.5°. Almost all types of oxazolones react with PhCH2NH2 to form α-acylaminoacyl-benzylamides. The reaction of V with d-MePhCHNH2 in dry dioxane was followed polarimetrically and at constant rotation, produced N-benzoylphenylalanine-d-N-α-phenylethylamide, m. 178-80°, [α]D23 28.5° (c 1, dioxane). The strongly enolyzed 2-phenyl-4-carbethoxy-5-oxazolone formed a salt with PhCH2NH2, converted on heating in xylene to the benzylamide, m. 132°. The reaction of

PhNH2.HCl with III and 2-benzyl-4-sec-butyl-5-oxazolone gave the normal anilide and the corresponding acid. Reaction of V and 2-phenyl-4-isobutyl-5-oxazolone with L-HSCH2CH-(NH2)CO2Me produced the normal amides, m. 128-9°, and 131-5°, resp., the NH2 group taking precedence over the SH group in the condensation. The action of N2H4 on oxazolones has been clarified. The addition of 18 g.-phenyl-4-methyl-5-oxazolone to excess 60% N2H4.H2O in EtOH and heating to 50-60° for 30 min. gave 17.5 g. benzoylalanine hydrazide, m. 142-4°; benzylidene derivative, m. 193-4°. Treatment of IV with N2H4.H2O also gave the normal hydrazide, PhCH:C(NHBz)CONHNH2, m. 113-14°, converted by heating the corresponding azide in xylene to 2-oxo-4-benzylidene-6-phenyl-1,3,5-oxadiazine, m. 174° (decomposition). Conversion of Me2C:C(NHBz)CON3 similarly produced 2-oxo-4-isopropylidene-6-phenyl-1,3,5-oxadiazine, m. 166-8°. A mixture of 5 g. IV, 10 mL. N2H4.H2O and 3 mL. EtOH was refluxed for 30 min. yielding 4-benzamido-3-phenyl-5-pyrazolidone, m. 228-9°, identical with the product formed by refluxing PhCH:C(NHBz)CONHNH2 (VIII), m. 157-8°, which N2H4.H2O for 30 min. Similarly, the hydrazide Me2C:C(NHBz)CONHNH2, m. 192-4°, was converted into 3,3-dimethyl-4-benzoylamino-5-pyrazolidine, m. 106-8°. The hydrazide VIII was boiled in N NaOH and the sparingly soluble salt on acidification gave 6-hydroxy-5-benzyl-3-phenyl-1,2,4-triazine, m. 175-6°; Ac derivative, 187-8°. Oxidation of XIII with K3Fe(CN)6 produced N,N'-bis(α-benzoylaminocinnamoyl)hydrazine, m. 265°, together with a substance, m. 186-7°, with the probable structure PhCH:C.CH(OH).NBz.C-(:CHPh).CH(OH).NBz, forming PhCH2CH(NHBz)-(CO2H) on alkaline hydrolysis. REACTIONS OF TYPE II OXAZOLONES: Some reactions involving the double bond in type II oxazolones have been discovered. Treatment of IV in dry dioxane with 2 mol CH2N2 in dry Et2O at 0° and allowing the solution to stand overnight at room temperature gave product, C17H13O2N, m. 142-3°. Addition of liquid NH3 to IVa with shaking and cooling in solid CO2 gave a small yield of basic product, C12H17O2N3, m. 162-6°, probably by addition of 2 mol NH3. Addition of H2S and RSH to the double bond has been studied in connection with various syntheses of penicillamine. The addition, of 136 g. IVa in 675 mL. dry benzene to 3.38 g. Na in 675 mL. of chilled dry MeOH and 76.5 mL. PhCH2SH produced Me2CC(NHBz)CO2Me, m. 137-8°, and Me2C(SCH2Ph)CH(NHBz)CO2Me, m. 66-7°. The addition probably takes place after ring opening, since the oxazolone can be replaced by an acrylic ester. Similarly, IV under like conditions, gave PhCH(SCH2Ph)CH-(NHBz)CO2Me, m. 164°. There is no evidence of direct addition of PhCH2SH to the double bond. Addition of H2S to IVa and VII in the presence of Et3N yielded Me2C(SH)CH(NHBz)COSH and Me2C(SH)CH(NHAc)COSH, resp. The initial step is probably the addition of H2S to the double bond. Anhydrous MeOH saturated with H2S at 0° treated with IVa gave 2,5,5-trimethyl-2-thiazoline-4-carboxylic acid, b25 120°; picrate, m. 159°, probably formed by addition, followed by displacement. IV similarly yielded 2-phenyl-5,5-dimethyl-2-thiazoline-4-carboxylic acid, m. 124-6°. IVa was apparently converted by treatment with alc. NaSH to 2-phenyl-4-isopropylidene-5-thiazolone, m. 100.5-101.5°. The reactivity of the Me groups in IVa is sufficient to permit condensation reactions with BzH to produce 2-phenyl-4-benzylideneisopropylidene-5-oxazolone, m. 135°. A mixture of stereoisomers, m. 134-6°, was produced by heating a mixture of 35.8 g. BzNHCH2CO2H, 32 g. PhCH:CHAc, 15 g. of fused NaOAc and 50 mL. Ac2O for 3 h. at 100°. IVa is a pseudo-acid and exhibits weak violet fluorescence in Et3N. On addition of NaOMe to IVa in MeOH, the initial intense blue-violet fluorescence in UV light due to the presence of the propenyl-oxazole soon disappears with the formation of Me2C:C(NHBz)CO2Me by ring opening. Miscellaneous REACTIONS OF OXAZOLONES. Excess PhMgBr was added to 6.0 g. 2-phenyl-4-methyl-5-oxazolone in Et2O and after refluxing for 6 h. the reaction product was hydrolyzed and extracted with Et2O, yielding 4.6 g. 1,1-diphenyl-2-benzoylamino-propanol, m. 192-3°. With AgClO4 in

benzene, III in EtOH gave a complex, m. 146° (decomposition). A similar crystalline compound, m. 172° (decomposition) was formed with 2-benzyl-4-methyl-5-oxazolone (IX). Formylation of 2,4-diphenyl-5-oxazolone apparently produced a stabilized enolic form, PhC:N.CPh:COH.O, m. 110°. Oxidation of 2-phenyl-4-isobutyl- and 2-phenyl-4-benzyl-5-oxazolones with Hg(OAc)2 gave the corresponding 4,4'-bisoxazolones, m. 138-42°, and 201-202.5°, resp. PSEUDO-OXAZOLONES. According to the method of Bergmann, 12 g. PhCHBrCONHCH2CO2H was added to 5 mL. dry pyridine and 100 mL. Ac2O and after 2.5 h. at 0° was poured over ice. The solid product was dried over NaOH and crystallized from warm MeOH by cooling to -50°, yielding 64% of 2-benzylidenepseudooxazolone (2-benzylidene-3-oxazolin-5-one), m. 92-4°, hydrolyzed by 0.5N HCl in acetone to PhCH2-CONH2, m. 153-7°. An attempt to prepare 2-benzyl-4-methylene-5-oxazolone by Bergmann's method from Ph-CHClCONHCHMeCO2H gave the potent skin irritant 2-benzylidene-4-methylpseudo-5-oxazolone (X), m. 105-115°, hydrolyzed by aqueous acetone to PhCH2CONH2 and AcCO2H, suggesting that the pseudooxazolones are intermediates in the Bermann synthesis of type II oxazolones and that, in general, the latter are in dynamic equilibrium with the pseudooxazolones. In an attempt to use pseudooxazolones for the thiazolidine-oxazolone structure suggested for penicillin, Br was added to V and the product condensed with penicillamine (XI) in the presence of AcOK and AcOH. The low order of activity noted was probably due to BrCH2COCO2H which has an activity of 6 units per mg. against Gram-pos. organisms. X (1 g.) in 40 mL. pure AcOEt was hydrogenated at several atmospheric pressure in the presence of 2 g. active Raney Ni to IX, suggesting that the thiazolidine-oxazolone structure might be accessible by reduction of the corresponding pseudooxazolone. Ice-cold pyridine (20 mL.) in 65 mL. Me2CO was mixed with 1 g. (EtO)2CHCH(NHCOCHBrPh)CO2H and after 3 h., the mixture was poured over crushed ice, extracted with CHCl3, washed with aqueous NaHCO3, dried by passage through acid-washed Al2O3, and the filtrate was evaporated, yielding 4.8 g. oily 2-benzylidene-4-(diethoxymethyl)pseudo-5-oxazolone, which failed to condense with XI. In another attempt, (EtO)2CHCH(NHCOCHClPh)CO2Me was condensed with XI to give α-Me α-chlorobenzylpenicilloate (XII). On treatment of crude XII (5.2 g.) with a mixture of 10.8 g. pyridine and 35.2 mL. Ac2O with shaking and cooling, a dark brown gum was formed, which, crystallized from Et2O at -50°, gave a "dehydropenicillin" (XIII), C16H16O4N2S, m. 90-5° (decomposition). Addnl. information in printed abstract

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FULL ESTIMATED COST                                      46.49      46.70

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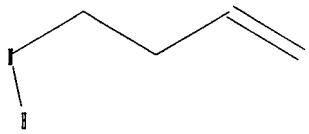

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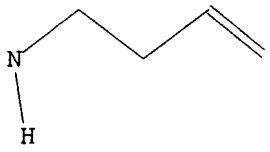

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SAMPLE SCREEN SEARCH COMPLETED - 32065 TO ITERATE

6.2% PROCESSED 2000 ITERATIONS 47 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 630594 TO 652006
PROJECTED ANSWERS: 13424 TO 16716

L11 47 SEA SSS SAM L10

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FULL SEARCH INITIATED 08:09:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 643047 TO ITERATE

100.0% PROCESSED 643047 ITERATIONS 13018 ANSWERS
SEARCH TIME: 00.00.03

L12 13018 SEA SSS FUL L10

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L13        5368 L12

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L4       714963 AMINO ACID
L5          433 L2(L)L4
L6      1459162 BETA
L7           82 L5 AND L6
L8       214408 ACETIC ACID
L9            5 L7 AND L8

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=> l8 and l15
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L18  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Improved method for synthesizing chiral or enantiomer-enriched beta-amino
     acids, -aldehydes, -ketones and gamma-amino alcohols
AN   2005:612232  CAPLUS
DN   143:133689
TI   Improved method for synthesizing chiral or enantiomer-enriched beta-amino
     acids, -aldehydes, -ketones and gamma-amino alcohols
IN   Walther, Jary; De Lange, Ben; Broxterman, Quirinus Bernardus; Pochlauer,
     Peter; Van der Sluis, Marcelles; Uiterweerd, Patrick; Falk, Heinz;
     Zuckerstatter, Gerhard
PA   DSM Fine Chemicals Austria Nfg G.m.b.H. & Co. K.-G., Austria
SO   PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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             NE, SN, TD, TG
                                             AT 2003-2051        A  20031219
                                             AT 2004-929         A  20040528
     EP 1694630          A1     20060830    EP 2004-820806           20041125
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                                             AT 2004-929         A  20040528
                                             WO 2004-EP13354     W  20041125
     US 2007123589       A1     20070531    US 2006-582671           20060612
                                             AT 2003-2051        A  20031219
                                             AT 2004-929         A  20040528
                                             WO 2004-EP13354     W  20041125
OS   CASREACT 143:133689; MARPAT 143:133689
AB   The title process consists of ozonolysis of allylamine derivs. in a
     solvent, followed by decomposition of the peroxide-containing solution by
means of an
     oxidizing agent or reductive reprocessing into the corresponding amino
     compound  Thus, (R)-4-amino-4-phenyl-1-butene was converted into
     (R)-3-amino-3-phenyl-1-propanol by ozonolysis in methanol at -20°,
     followed by treatment with sodium borohydride, distillation of solvent, and
     workup of the product.  Product was obtained in 93% yield with 99%
     enantio-purity; m.p. 73-74°.
RE.CNT  6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

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TI   A diastereoselective synthesis of the tetrahydropyridazinone core of
     2-oxo-1,6-diazobicyclo[4.3.0]nonane-9-carboxylate-based peptidomimetics
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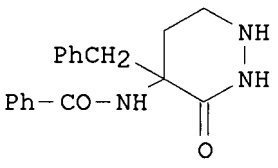
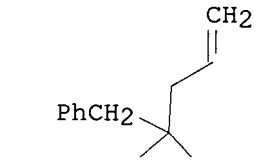
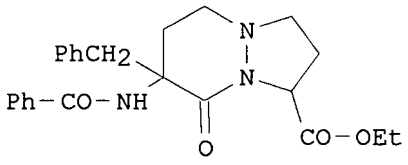
starting from (S)-phenylalanine
AN 2003:345327 CAPLUS
DN 139:53299
TI A diastereoselective synthesis of the tetrahydropyridazinone core of 2-oxo-1,6-diazobicyclo[4.3.0]nonane-9-carboxylate-based peptidomimetics starting from (S)-phenylalanine
AU Gardiner, James; Abell, Andrew D.
CS Department of Chemistry, University of Canterbury, Christchurch, N. Z.
SO Tetrahedron Letters (2003), 44(22), 4227-4230
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 139:53299
GI



I



II



III

AB A diastereoselective synthesis of the peptidic tetrahydropyridazinone I from (S)-phenylalanine via ozonolysis and reduction of the dialkylated amino acid II. I can be converted via 1,3-dipolar cycloaddn. to the bicyclic peptidomimetic III, an important class of β-strand mimetic serine proteases inhibitors.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.78	233.03
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.56	-6.24

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FILE 'CAPLUS' ENTERED AT 08:23:27 ON 14 JUN 2007
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.78	233.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.56	-6.24

=> file scisearch

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.78	233.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.56	-6.24

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
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SCISEARCH has been reloaded, see HELP RLOAD for details.

=> s goering H L/RAU (S) 70/RVL (S)3310/RPG
1650 GOERING H L/RAU
1597369 70/RVL
9497 3310/RPG
L19 10 GOERING H L/RAU (S) 70/RVL (S)3310/RPG

=> d l19 1-5 all

L19 ANSWER 1 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2005:995712 SCISEARCH
GA The Genuine Article (R) Number: 968MO
TI Synthesis of oxytocin analogues with replacement of sulfur by carbon gives potent antagonists with increased stability
AU Stymiest J L; Mitchell B F; Wong S; Vederas J C (Reprint)
CS Univ Alberta, Dept Chem, Edmonton, AB T6G 2G2, Canada (Reprint); Univ Alberta, Dept Obstet & Gynecol, Perinatal Res Ctr, Edmonton, AB TH5 3V9, Canada
CYA Canada
SO JOURNAL OF ORGANIC CHEMISTRY, (30 SEP 2005) Vol. 70, No. 20, pp. 7799-7809.
ISSN: 0022-3263.
PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

DT Article; Journal
LA English
REC Reference Count: 61
ED Entered STN: 13 Oct 2005
Last Updated on STN: 1 Dec 2005

AB The neuropeptide oxytocin 1 controls mammary and uterine smooth muscle contraction. Atosiban 2, an oxytocin antagonist, is used for prevention of preterm labor and premature birth. However, the metabolic lifetimes of such peptide drugs are short because of in vivo degradation. Facile production of oxytocin analogues with varying ring sizes wherein sulfur is replaced by carbon (methylene or methine) could be achieved by standard solid-phase peptide synthesis using olefin-bearing amino acids followed by on-resin ring-closing metathesis (RCM). These were tested for agonistic and antagonistic uteronic activity using myometrial strips taken from nonpregnant female rats. Peptide 8 showed agonistic activity in vitro (EC50 = 1.4 x 10(3) +/- 4.4 x 10(2) nM) as compared to 1 (EC50 = 7.0 +/- 2.1 nM). Atosiban analogues 17 (pA(2) = 7.8 +/- 0.1) and 18 (pA(2) 8.0 +/- 0.1) showed substantial activity compared to the parent oxytocin antagonist 2 (pA(2) = 9.9 +/- 0.3). Carba analogue 35 (pA(2) = 6.1 +/- 0.1) had an agonistic activity over 2 orders of magnitude less than its parent 3 (8.8 +/- 10.5). A comparison of biological stabilities of 1,6-carba analogues of both an agonist 8 and antagonist 18 versus parent peptides 1 and 2 was conducted. The half-lives of peptides 8 and 18 in rat placental tissue were shown (Table 2) to be greatly improved versus their parents oxytocin 1 and atosiban 2, respectively. These results suggest that peptides 8 and 18 and analogues thereof may be important leads into the development of a long-lasting, commercially available therapeutic for initiation of parturition and treatment of preterm labor.

CC CHEMISTRY, ORGANIC

STP KeyWords Plus (R): RING-CLOSING METATHESIS; PRETERM LABOR; BENZOFURAN DERIVATIVES; METABOLIC STABILITY; OLEFIN METATHESIS; DICARBA ANALOGS; LACTAM ANALOGS; DOUBLE-BLIND; AMINO-ACIDS; ATOSIBAN

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
CABROL D	2001	98	177	EUR J OBSTET GYN R B	
MOUTQUIN J M	2001	108	133	BRIT J OBSTET GYNAEC	
ANDERSSON K E	1983	26	56	CLIN OBSTET GYNECOL	
BALDWIN J E	1992	6	1517	J CHEM RES MINIPRINT	
BIAGINI S C	1998	116	2485	J CHEM SOC P1	
BROUWER A J	2004	69	3662	J ORG CHEM	
CALLAHAN J F	1988	53	1527	J ORG CHEM	
CIRILLO R	2003	306	253	J PHARMACOL EXP THER	
ENGSTROM T	1998	355	203	J PHARM	
EVANS B E	1992	35	3919	J MED CHEM	
GAL C S L	2004	309	414	J PHARMACOL EXP THER	
GAO Y	2001	3	1617	ORG LETT	
GAZAL S	2002	45	1665	J MED CHEM	
GAZIS D	1978	158	663	P SOC EXP BIOL MED	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--
GOLDENBERG R L	1998	339	313	NEW ENGL J MED	
GOODWIN T M	1994	170	474	AM J OBSTET GYNECOL	
GOODWIN T M	2001	11	339	J SOC GYNECOL INVEST	
GRIECO P	2002	10	3731	BIOORGAN MED CHEM	
GYETVAI K	1999	94	869	OBSTET GYNECOL S 2	
HARGITTAI B	2000	43	4787	J MED CHEM	
HARRIS J C	1998	156	35	J ENDOCRINOL	
HAVASS J	2002	23	1419	PEPTIDES	
HIGBY K	1999	21	35	DRUG SAFETY	
JARVO E R	1999	121	11638	J AM CHEM SOC	
KASMAIER U	1999	1	1763	ORG LETT	
KELLER O	1974	57	1253	HELV CHIM ACTA	

KUO M S	1998	8	3081	BIOORG MED CHEM LETT
MANNING M	2001	7	449	J PEPT SCI
MELIN P	1986	111	125	J ENDOCRINOL
MILLER S J	1996	118	9606	J AM CHEM SOC
MITCHELL B F	1997	57	807	BIOL REPROD
MOUTQUIN J M	2000	182	1191	AM J OBSTET GYNECOL
NELSON R	2004	104	23	AM J NURS
NICHOLSON H D	1996	1	69	REV REPROD
RAMTOHUL Y K	2002		192	THESIS U ALBERTA
REICHWEIN J F	2000		2335	EUR J ORG CHEM JUN
REICHWEIN J F	2000	65	6187	J ORG CHEM
SCHAFMEISTER C E	2000	122	5891	J AM CHEM SOC
SCHILD H O	1947	2	189	BRIT J PHARMACOL
SCHMIEDEBERG N	2002	4	59	ORG LETT
SCHOLL M	1999	1	953	ORG LETT
SCHWAB P	1996	118	100	J AM CHEM SOC
SCHWAB P	1995	34	2039	ANGEW CHEM INT EDIT
SERVITOVA L	1975	40	215	COLLECT CZECH CHEM C
SILVERSTEIN R M	1998			SPECTROMETRIC IDENTI
SMITH C W	1976	19	250	J MED CHEM
SMITH C W	1978	21	117	J MED CHEM
SPANTULESCU M D	2003	5	2963	ORG LETT
SPINELLA M J	1991	88	7443	P NATL ACAD SCI USA
STYMIEST J L	2003	5	47	ORG LETT
SWEETMAN S C	2004			MARTINDALE COMPLETE
TAUNTON J	1996	118	10412	J AM CHEM SOC
THRUIEAU C	1995	30	115	EUR J MED CHEM
TSATSARIS V	2004	64	375	DRUGS
VILLAR J	1994	16	9	RES CLIN FORUMS
WILLIAMS P D	1999	9	1311	BIOORG MED CHEM LETT
WILLIAMS R M	1998	63	2130	J ORG CHEM
WILSON L	1990	163	195	AM J OBSTET GYNECOL
WYATT P G	2002	12	1405	BIOORG MED CHEM LETT
WYATT P G	2002	12	1399	BIOORG MED CHEM LETT

L19 ANSWER 2 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1997:518782 SCISEARCH

GA The Genuine Article (R) Number: XH601

TI Reactivity of alpha-unsaturated organozinc compounds with N-(phenylsulfanyl)iminoesters - Application to the synthesis of monosubstituted or disubstituted unsaturated alpha-aminoacids

AU Aidene M (Reprint); Barbot F; Miginiac L

CS UNIV POITIERS, ORGAN SYNTH LAB, CNRS, URA 574, F-86022 POITIERS, FRANCE

CYA FRANCE

SO JOURNAL OF ORGANOMETALLIC CHEMISTRY, (28 APR 1997) Vol. 534, No. 1-2, pp. 117-127.
ISSN: 0022-328X.

PB ELSEVIER SCIENCE SA LAUSANNE, PO BOX 564, 1001 LAUSANNE, SWITZERLAND.

DT Article; Journal

FS PHYS

LA French

REC Reference Count: 39

ED Entered STN: 1997
Last Updated on STN: 1997

AB A new general synthesis of C-subtituted alpha-aminoacids is described, using at first the regioselective reaction between alpha-unsaturated organozincs and N-(phenylsulfanyl)iminoesters.

CC CHEMISTRY, INORGANIC & NUCLEAR; CHEMISTRY, ORGANIC

ST Author Keywords: N-(phenylsulfanyl)iminoesters; regioselectivity; allylic organozincs; allenic organozincs; alpha-aminoesters; alpha-aminoacide

STP KeyWords Plus (R): CHIRAL AUXILIARIES; 3-AMINO ALCOHOLS; ACID; REGIOSELECTIVITY; REAGENTS; 2-(BROMOMETHYL)ACRYLATES; IMINOESTERS;

ALKYLATION; SECONDARY; 2-AMINO

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
ABOOD N A	1994	35	3669	TETRAHEDRON LETT	
BARBOT F	1981		4016	J CHEM RES M	
BARBOT F	1981		343	J CHEM RES S	
BENATI L	1986	27	1739	TETRAHEDRON LETT	
BHATTACHARJEE S K	1981	50	813	CURRENT SCI	
BUNUEL E	1992		579	SYNLETT	
CHAN L H	1967	9	231	J ORGANOMET CHEM	
COURTOIS G	1989	376	235	J ORGANOMET CHEM	
COURTOIS G	1993	450	33	J ORGANOMET CHEM	
COURTOIS G	1993	452	5	J ORGANOMET CHEM	
DAVIS F A	1977	42	398	J ORG CHEM	
DEMBELE Y A	1992	3	351	TETRAHEDRON-ASYMMETR	
DEMBELE Y A	1992	3	511	TETRAHEDRON-ASYMMETR	
DJURIC S	1981	22	1787	TETRAHEDRON LETT	
FILLMAN J	1948	70	171	J AM CHEM SOC	
FRONZA G	1983	2	225	J CARBOHYD CHEM	
GAUDEMAR M	1962		974	B SOC CHIM FR	
GAUDEMAR M	1963		1475	B SOC CHIM FR	
GENET J P	1988	44	5263	TETRAHEDRON	
GENET J P	1992	33	2497	TETRAHEDRON LETT	
GERSHON H	1954	76	3484	J AM CHEM SOC	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--
GORDON E M	1977	99	5504	J AM CHEM SOC	
GORDON E M	1980	102	1690	J AM CHEM SOC	
GORDON E M	1979	44	1218	J ORG CHEM	
GUO Z X	1993		874	J CHEM SOC CHEM COMM	
HARPP D N	1971		4953	TETRAHEDRON LETT	
HASEGAWA H	1993		489	J CHEM SOC PERK T 1	
HIRAO A	1982		461	SYNTHESIS-STUTTGART	
KOBAYASHI T	1979	27	2718	CHEM PHARM BULL	
KOBAYASHI T	1977	99	5505	J AM CHEM SOC	
LADURANTY J	1987	65	859	CAN J CHEM	
LOVEY R G	1994		167	SYNLETT	
MOREAU J L	1970		2171	B SOC CHIM FR	
MOREAU J L	1980		363	CHEM KETENES ALLEN 1	
MUKAIYAMA T	1970		3411	TETRAHEDRON LETT	
PARKER E D	1961	236	3267	J BIOL CHEM	
SURZUR J M	1969	269	849	CR ACAD SCI C CHIM	
YANG T K	1994	59	914	J ORG CHEM	

L19 ANSWER 3 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1995:374653 SCISEARCH

GA The Genuine Article (R) Number: RA830

TI 2 SIMILAR LACTONE-HYDROCHLORIDES WITH DIFFERENT TYPES OF HYDROGEN-BONDING NETWORKS - CRYSTAL-STRUCTURE OF (R,S)-ALPHA-AMINO-GAMMA-CAPROLACTONE HYDROCHLORIDE AND RACEMIC ALPHA-AMINO-GAMMA-METHYL-GAMMA-VALEROLACTONE HYDROCHLORIDE SEMIHYDRATE

AU KAITNER B (Reprint); KIRIN S I; MESTROVIC E

CS UNIV ZAGREB, FAC SCI, DEPT CHEM, POB 153, ZVONIMIROVA 8, ZAGREB 41001, CROATIA (Reprint); RUDJER BOSKOVIC INST, ZAGREB 41001, CROATIA

CYA CROATIA

SO JOURNAL OF CHEMICAL CRYSTALLOGRAPHY, (MAR 1995) Vol. 25, No. 3, pp. 117-122.
ISSN: 1074-1542.

PB PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013.

DT Article; Journal

FS PHYS

LA English
REC Reference Count: 24
ED Entered STN: 1995
Last Updated on STN: 1995
AB The X-ray crystal structure of (R,S)-alpha-amino-gamma-caprolactone hydrochloride (compound 1) and alpha-amino-gamma-methyl-gamma-valerolactone hydrochloride semihydrate (compound 2) are presented. Both compound 1 and compound 2 belong to the orthorhombic system. Caprolactone-hydrochloride 1 crystallizes in the space group P2(1)2(1)2(1) with a = 5.1948(7), b = 8.7404(8), c = 17.907(1) Angstrom, V = 813.0(2) Angstrom(3), Z = 4. Valerolactone-hydrochloride 2 crystallizes in the space group Pna2(1) with a = 26.771(8), b = 5.1598(7), c = 13.201(3) Angstrom, V = 1823.5(7) Angstrom(3), Z = 8. The lactone cations maintain the same, open envelope conformation in both crystals. The lactone-hydrochloride packing arrangements in 1 and 2 are distinctly different. While in 1 N-H ... Cl and N-H ... O hydrogen bonding creates two dimensional nets in the form of puckered layers perpendicular to the [001] direction, in 2 a water molecule of crystallization with an additional OW-H ... Cl hydrogen interaction assists in forming a three-dimensional hydrogen-bond network throughout the crystal.
CC CRYSTALLOGRAPHY; SPECTROSCOPY
ST Author Keywords: LACTONE-HYDROCHLORIDE; SOLID-STATE STRUCTURE; X-RAY DIFFRACTION; CONFORMATION
STP KeyWords Plus (R): NEUTRON-DIFFRACTION; SYSTEM
RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
ANON	1992			DIF4 DIFFRACTOMETER	
ANON	1992			REDU4 DATA REDUCTION	
ALCOCK, N W	1989	21	1835	PHYTOCHEMISTRY	
ALLEN, F H	1987		S1	J CHEM SOC PERK T 2	
ARMSTRONG, M D	1949	71	3399	J AM CHEM SOC	
BOCELLI, G	1981	37	2106	ACTA CRYSTALLOGR SOC	
BRUVO, M	1981	37	700	ACTA CRYSTALLOGR B	
DELJAC, A	1993	49	1354	ACTA CRYSTALLOGR C	
FILLMAN, J	1948	70	171	J AM CHEM SOC	
GABE, E J	1989	22	384	J APPL CRYSTALLOGR	
GOERING, H L	1948	70	3310	J AM CHEM SOC	<--
IBERS, J A	1974	4	99	INT TABLES XRAY CRYS	
JOHNSON, C K	1976			ORNL5138 REP	
KAITNER, B	1994			UNPUB STRUCT CHEM	
KIRIN, S I	1993		120	13TH M CROAT CHEM ZA	
MATIJASIC, I	1988	44	159	ACTA CRYSTALLOGR	
MATIJASIC, I	1989	45	1546	ACTA CRYSTALLOGR C	
MO, F	1971	27	115	ACTA CRYSTALLOGR B	
NARDELLI, M	1983	7	95	COMPUT CHEM	
PAPAIOANNOU, D	1990	44	189	ACTA CHEM SCAND	
ROGERS, D	1981	37	734	ACTA CRYSTALLOGR A	
STEINER, T	1993	115	4540	J AM CHEM SOC	
USHER, J J	1978	34	2012	ACTA CRYSTALLOGR B	
WALKER, N	1983	39	158	ACTA CRYSTALLOGR A	

L19 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1992:670958 SCISEARCH
GA The Genuine Article (R) Number: JX822
TI SYNTHESIS OF (OPTICALLY-ACTIVE) SULFUR-CONTAINING TRIFUNCTIONAL AMINO-ACIDS BY RADICAL-ADDITION TO (OPTICALLY-ACTIVE) UNSATURATED AMINO-ACIDS
AU BROXTERMAN Q B (Reprint); KAPTEIN B; KAMPHUIS J; SCHOEMAKER H E
CS DSM RES & PATENTS, BIOORGAN CHEM SECT, POB 18, 6160 MD GELEEN, NETHERLANDS (Reprint)

CYA NETHERLANDS
SO JOURNAL OF ORGANIC CHEMISTRY, (6 NOV 1992) Vol. 57, No. 23, pp. 6286-6294. ISSN: 0022-3263.
PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DT Article; Journal
FS PHYS; LIFE
LA English
REC Reference Count: 42
ED Entered STN: 1994
Last Updated on STN: 1994
AB Sulfur-based radicals, generated from R-S-H-type precursors (R = alkyl, acyl) with AIBN, smoothly add to alpha-allylglycines protected at none, one, or both of the amino acid functions (NH2 and/or CO2H). Sulfur-containing trifunctional amino acids were obtained in good to excellent yields (64-100%). The solvent used for the reaction is critical. Optimal results were obtained when both the unsaturated amino acid and RSH dissolve completely in the medium (dioxane/water or methanol/water are good solvent systems). The scope of the reaction includes alpha-substituted alpha-allylglycine and derivatives as well as beta-substituted beta-allyl-beta-ammo alcohols. In the case of optically active alpha-allylglycine derivatives, radical addition is accompanied by a small amount of racemization, the amount depending on the type of protection and R-S-H. The products are easily optically enriched by crystallization. Addition of sulfur-based radicals to alpha-allylglycine is believed to be an example of a general method for synthesizing optically active trifunctional amino acids from unsaturated amino acids.
CC CHEMISTRY, ORGANIC
STP KeyWords Plus (R): ENANTIOSELECTIVE SYNTHESIS; N-ACYLOXAZOLIDINONES; ASYMMETRIC-SYNTHESIS; DERIVATIVES; DEHYDROALANINE
RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
ADLINGTON, R M	1983		94	J CHEM OC CHEM COMMU	
ALBERTSON, N F	1946	68	450	J AM CHEM SOC	
BALDWIN, J E	1988		1031	J CHEM SOC CHEM COMM	
BARTON, D H R	1988	44	5479	TETRAHEDRON	
BECKWITH, A L J	1990		1087	J CHEM SOC CHEM COMM	
BELOKON, Y N	1985		171	J CHEM SOC CHEM COMM	
BOESTEN, W H J	1986	178	355	NATO ASI SER C-MATH	
BOLM, C	1991	103	566	ANGEW CHEM	
BURGER, K	1991	115	328	CHEM ZTG	
COREY, E J	1991	56	442	J ORG CHEM	
CRICH, D	1988		140	J CHEM RES SYNOP	
CRICH, D	1989	45	5641	TETRAHEDRON	
EASTON, C J	1991	56	5614	J ORG CHEM	
ESCH, P M	1990	31	759	TETRAHEDRON LETT	
EVANS, D A	1991	56	5750	J ORG CHEM	
GAGE, J R	1989	68	77	ORG SYNTH	
GIESE, B	1986			RADICALS ORGANIC SYN	
GOERING, H L	1948	70	3310	J AM CHEM SOC	<--
KAPTEIN, B				IN PRESS TETRAHEDRON	
KATAGIRI, N	1991		1429	J CHEM SOC CHEM COMM	
KJAER, A	1955	9	721	ACTA CHEM SCAND	
KRUIZINGA, W H	1988	53	1826	J ORG CHEM	
LOGUSCH, E W	1988	29	6055	TETRAHEDRON LETT	
MEIJER, E M	1985		135	BIOCATALYSTS ORGANIC	
MEYERS, A I	1991	56	7098	J ORG CHEM	
MIYAZAWA, T	1991	6	887	CHEM EXPRESS	
NEFKENS, G H L	1960	79	688	RECL TRAV CHIM PAY B	
SANDLER, M	1989			DESIGN ENZYME INHIBI	
SCHOLLKOPF, U	1981		969	SYNTHESIS-STUTTGART	
SNIDER, B B	1991	56	4908	J ORG CHEM	

SOAI, K	1991	2	781	TETRAHEDRON-ASYMMETR
SORENSEN, S P L	1902	6	137	COMPT REND TRAV LAB
TOMIOKA, K	1991	32	3095	TETRAHEDRON LETT
URBACH, H	1989	28	957	HETEROCYCLES
VRIESEMA, B K	1986	26	2045	TETRAHEDRON LETT
WALKER, M A	1991	56	5747	J ORG CHEM
WILLIAMS, R M	1991	113	9276	J AM CHEM SOC
ZEISS, H J	1990			7TH INT C PEST CHEM

STN Patent No. (RPN)	Year (RPY)	Ref. Inventor/Assignee (RIN)	Type	Ref. Patent No. (RPN)
1548032	1976	BOESTEN, W H J		1548032
DE 3817956		ZEISS, H J	APPL	GE 3817956
US 3971700	1976	BOESTEN, W H J		US 3971700
US 4172846	1979	BOESTEN, W H J		US 4172846

L19 ANSWER 5 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1992:394911 SCISEARCH
GA The Genuine Article (R) Number: JA979
TI 2-AMINO-4-TRIMETHYLSILYL-GAMMA-BUTYROLACTONE - A SILYL ANALOGOUS HOMOTHREONINE LACTONE
AU EBELING S (Reprint); MATTHIES D; MCCARTHY D
CS UNIV HAMBURG, INST PHARMACEUT CHEM, BUNDESSTR 45, W-2000 HAMBURG 13, GERMANY
CYA GERMANY
SO JOURNAL FUR PRAKTISCHE CHEMIE-CHEMIKER-ZEITUNG, (1992) Vol. 334, No. 4, pp. 361-362.
ISSN: 0941-1216.
PB JOHANN AMBROSIUS BARTH VERLAG, IM WEIHER 10, D-69121 HEIDELBERG, GERMANY.
DT Article; Journal
FS PHYS; ENGI
LA German
REC Reference Count: 8
ED Entered STN: 1994
Last Updated on STN: 1994
CC CHEMISTRY; CHEMISTRY, APPLIED
STP KeyWords Plus (R): AMINO-ACIDS; DERIVATIVES; LACTONIZATION
RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
BENISHAI, D	1977	33	1533	TETRAHEDRON	
CHENAULT, H K	1989	111	6354	J AM CHEM SOC	
EBELING, S	1991	60	265	PHOSPHORUS SULFUR	
GOERING, H L	1948	70	3310	J AM CHEM SOC	<--
KUROKAWA, N	1986	108	6041	J AM CHEM SOC	
OHFUNE, Y	1985	26	5307	TETRAHEDRON LETT	
OHFUNE, Y	1986	27	6079	TETRAHEDRON LETT	
WILLIAMS, R M	1988	110	1547	J AM CHEM SOC	

=> d 1-10 ibib abs hit

L19 ANSWER 1 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:995712 SCISEARCH
THE GENUINE ARTICLE: 968MO
TITLE: Synthesis of oxytocin analogues with replacement of sulfur by carbon gives potent antagonists with increased stability
AUTHOR: Stymiest J L; Mitchell B F; Wong S; Vederas J C (Reprint)

CORPORATE SOURCE: Univ Alberta, Dept Chem, Edmonton, AB T6G 2G2, Canada (Reprint); Univ Alberta, Dept Obstet & Gynecol, Perinatal Res Ctr, Edmonton, AB TH5 3V9, Canada
COUNTRY OF AUTHOR: Canada
SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (30 SEP 2005) Vol. 70, No. 20, pp. 7799-7809.
ISSN: 0022-3263.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 61
ENTRY DATE: Entered STN: 13 Oct 2005
Last Updated on STN: 1 Dec 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The neuropeptide oxytocin 1 controls mammary and uterine smooth muscle contraction. Atosiban 2, an oxytocin antagonist, is used for prevention of preterm labor and premature birth. However, the metabolic lifetimes of such peptide drugs are short because of in vivo degradation. Facile production of oxytocin analogues with varying ring sizes wherein sulfur is replaced by carbon (methylene or methine) could be achieved by standard solid-phase peptide synthesis using olefin-bearing amino acids followed by on-resin ring-closing metathesis (RCM). These were tested for agonistic and antagonistic uteronic activity using myometrial strips taken from nonpregnant female rats. Peptide 8 showed agonistic activity in vitro (EC50 = 1.4 x 10(3) +/- 4.4 x 10(2) nM) as compared to 1 (EC50 = 7.0 +/- 2.1 nM). Atosiban analogues 17 (pA(2) = 7.8 +/- 0.1) and 18 (pA(2) 8.0 +/- 0.1) showed substantial activity compared to the parent oxytocin antagonist 2 (pA(2) = 9.9 +/- 0.3). Carba analogue 35 (pA(2) = 6.1 +/- 0.1) had an agonistic activity over 2 orders of magnitude less than its parent 3 (8.8 +/- 10.5). A comparison of biological stabilities of 1,6-carba analogues of both an agonist 8 and antagonist 18 versus parent peptides 1 and 2 was conducted. The half-lives of peptides 8 and 18 in rat placental tissue were shown (Table 2) to be greatly improved versus their parents oxytocin 1 and atosiban 2, respectively. These results suggest that peptides 8 and 18 and analogues thereof may be important leads into the development of a long-lasting, commercially available therapeutic for initiation of parturition and treatment of preterm labor.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
GOERING H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 2 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:518782 SCISEARCH
THE GENUINE ARTICLE: XH601
TITLE: Reactivity of alpha-unsaturated organozinc compounds with N-(phenylsulfanyl)iminoesters - Application to the synthesis of monosubstituted or disubstituted unsaturated alpha-aminoacids
AUTHOR: Aidene M (Reprint); Barbot F; Miginiac L
CORPORATE SOURCE: UNIV POITIERS, ORGAN SYNTH LAB, CNRS, URA 574, F-86022 POITIERS, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: JOURNAL OF ORGANOMETALLIC CHEMISTRY, (28 APR 1997) Vol. 534, No. 1-2, pp. 117-127.
ISSN: 0022-328X.
PUBLISHER: ELSEVIER SCIENCE SA LAUSANNE, PO BOX 564, 1001 LAUSANNE, SWITZERLAND.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: French

REFERENCE COUNT: 39
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A new general synthesis of C-subtituted alpha-aminoacids is described, using at first the regioselective reaction between alpha-unsaturated organozincs and N-(phenylsulfanyl)iminoesters.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--

L19 ANSWER 3 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:374653 SCISEARCH
THE GENUINE ARTICLE: RA830
TITLE: 2 SIMILAR LACTONE-HYDROCHLORIDES WITH DIFFERENT TYPES OF HYDROGEN-BONDING NETWORKS - CRYSTAL-STRUCTURE OF (R,S)-ALPHA-AMINO-GAMMA-CAPROLACTONE HYDROCHLORIDE AND RACEMIC ALPHA-AMINO-GAMMA-METHYL-GAMMA-VALEROLACTONE HYDROCHLORIDE SEMIHYDRATE
AUTHOR: KAITNER B (Reprint); KIRIN S I; MESTROVIC E
CORPORATE SOURCE: UNIV ZAGREB, FAC SCI, DEPT CHEM, POB 153, ZVONIMIROVA 8, ZAGREB 41001, CROATIA (Reprint); RUDJER BOSKOVIC INST, ZAGREB 41001, CROATIA
COUNTRY OF AUTHOR: CROATIA
SOURCE: JOURNAL OF CHEMICAL CRYSTALLOGRAPHY, (MAR 1995) Vol. 25, No. 3, pp. 117-122.
ISSN: 1074-1542.
PUBLISHER: PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 24
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The X-ray crystal structure of (R,S)-alpha-amino-gamma-caprolactone hydrochloride (compound 1) and alpha-amino-gamma-methyl-gamma-valerolactone hydrochloride semihydrate (compound 2) are presented. Both compound 1 and compound 2 belong to the orthorhombic system. Caprolactone-hydrochloride 1 crystallizes in the space group P2(1)2(1)2(1) with a = 5.1948(7), b = 8.7404(8), c = 17.907(1) Angstrom, V = 813.0(2) Angstrom(3), Z = 4. Valerolactone-hydrochloride 2 crystallizes in the space group Pna2(1) with a = 26.771(8), b = 5.1598(7), c = 13.201(3) Angstrom, V = 1823.5(7) Angstrom(3), Z = 8. The lactone cations maintain the same, open envelope conformation in both crystals. The lactone-hydrochloride packing arrangements in 1 and 2 are distinctly different. While in 1 N-H ... Cl and N-H ... O hydrogen bonding creates two dimensional nets in the form of puckered layers perpendicular to the [001] direction, in 2 a water molecule of crystallization with an additional OW-H ... Cl hydrogen interaction assists in forming a three-dimensional hydrogen-bond network throughout the crystal.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING, H L	1948	70	3310	J AM CHEM SOC	<--

L19 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:670958 SCISEARCH
THE GENUINE ARTICLE: JX822
TITLE: SYNTHESIS OF (OPTICALLY-ACTIVE) SULFUR-CONTAINING

TRIFUNCTIONAL AMINO-ACIDS BY RADICAL-ADDITION TO (OPTICALLY-ACTIVE) UNSATURATED AMINO-ACIDS

AUTHOR: BROXTERMAN Q B (Reprint); KAPTEIN B; KAMPHUIS J; SCHOEMAKER H E

CORPORATE SOURCE: DSM RES & PATENTS, BIOORGAN CHEM SECT, POB 18, 6160 MD GELEEN, NETHERLANDS (Reprint)

COUNTRY OF AUTHOR: NETHERLANDS

SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (6 NOV 1992) Vol. 57, No. 23, pp. 6286-6294.
ISSN: 0022-3263.

PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; LIFE

LANGUAGE: English

REFERENCE COUNT: 42

ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sulfur-based radicals, generated from R-S-H-type precursors (R = alkyl, acyl) with AIBN, smoothly add to alpha-allylglycines protected at none, one, or both of the amino acid functions (NH2 and/or CO2H). Sulfur-containing trifunctional amino acids were obtained in good to excellent yields (64-100%). The solvent used for the reaction is critical. Optimal results were obtained when both the unsaturated amino acid and RSH dissolve completely in the medium (dioxane/water or methanol/water are good solvent systems). The scope of the reaction includes alpha-substituted alpha-allylglycine and derivatives as well as beta-substituted beta-allyl-beta-ammo alcohols. In the case of optically active alpha-allylglycine derivatives, radical addition is accompanied by a small amount of racemization, the amount depending on the type of protection and R-S-H. The products are easily optically enriched by crystallization. Addition of sulfur-based radicals to alpha-allylglycine is believed to be an example of a general method for synthesizing optically active trifunctional amino acids from unsaturated amino acids.

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
GOERING, H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 5 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:394911 SCISEARCH

THE GENUINE ARTICLE: JA979

TITLE: 2-AMINO-4-TRIMETHYLSILYL-GAMMA-BUTYROLACTONE - A SILYL ANALOGOUS HOMOTHREONINE LACTONE

AUTHOR: EBELING S (Reprint); MATTHIES D; MCCARTHY D

CORPORATE SOURCE: UNIV HAMBURG, INST PHARMACEUT CHEM, BUNDESSTR 45, W-2000 HAMBURG 13, GERMANY

COUNTRY OF AUTHOR: GERMANY

SOURCE: JOURNAL FUR PRAKTISCHE CHEMIE-CHEMIKER-ZEITUNG, (1992) Vol. 334, No. 4, pp. 361-362.
ISSN: 0941-1216.

PUBLISHER: JOHANN AMBROSIUS BARTH VERLAG, IM WEIHER 10, D-69121 HEIDELBERG, GERMANY.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS; ENGI

LANGUAGE: German

REFERENCE COUNT: 8

ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)

GOERING, H L |1948 |70 |3310 |J AM CHEM SOC <--

L19 ANSWER 6 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1983:197377 SCISEARCH
THE GENUINE ARTICLE: QL720
TITLE: TRITIATED PEPTIDES .13. SYNTHESIS OF [4,5-H-3-LEU2]-LOCUST AND [3,4-H-3-PROG]-LOCUST ADIPOKINETIC HORMONE
AUTHOR: HARDY P M (Reprint); SHEPPARD P W; BRUNDISH D E; WADE R
CORPORATE SOURCE: CIBA GEIGY, RES CTR, DIV PHARMACEUT, HORSHAM RH12 4AB, W SUSSEX, ENGLAND; UNIV EXETER, DEPT CHEM, EXETER EX4 4QD, DEVON, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-PERKIN TRANSACTIONS 1, (1983) No. 4, pp. 731-734.
ISSN: 0300-922X.
PUBLISHER: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK, MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 12
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
GOERING, H L	1948	70	3310	J AM CHEM SOC <--

L19 ANSWER 7 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1979:157628 SCISEARCH
THE GENUINE ARTICLE: GR232
TITLE: MOLECULAR-SPECIES OF SCHIFF-BASES DERIVED FROM ORTHO-HYDROXYAROMATIC ALDEHYDES .3. SCHIFF-BASES OF PYRIDOXAL AND ITS ANALOGS WITH UNSATURATED AMINO-ACIDS
AUTHOR: MATSUSHIMA Y (Reprint); KARUBE Y; KONO A
CORPORATE SOURCE: KYUSHU UNIV, FAC PHARMACEUT SCI, HIGASHI KU, FUKUOKA 812, JAPAN (Reprint); KYUSHU CANC CTR RES INST, MINAMI KU, FUKUOKA 815, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: CHEMICAL & PHARMACEUTICAL BULLETIN, (1979) Vol. 27, No. 3, pp. 703-709.
ISSN: 0009-2363.
PUBLISHER: PHARMACEUTICAL SOC JAPAN, 2-12-15-201 SHIBUYA, SHIBUYA-KU, TOKYO 150, JAPAN.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 24
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
GOERING, H L	1948	70	3310	J AM CHEMICAL SOC <--

L19 ANSWER 8 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1977:254549 SCISEARCH
THE GENUINE ARTICLE: DK728
TITLE: NEW SYNTHESIS OF AMINO-ACIDS .2. AMIDOALKYLATION OF OLEFINS WITH GLYOXYLIC-ACID DERIVATIVES

AUTHOR: BENISHAI D (Reprint); MOSHENBERG R; ALTMAN J
CORPORATE SOURCE: TECHNION ISRAEL INST TECHNOL, DEPT CHEM, HAIFA, ISRAEL
COUNTRY OF AUTHOR: ISRAEL
SOURCE: TETRAHEDRON, (1977) Vol. 33, No. 12, pp. 1533-1542.
ISSN: 0040-4020.
PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 24
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING, H L	1948	70	3310	J AM CHEM SOC	<--

L19 ANSWER 9 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1975:385412 SCISEARCH
THE GENUINE ARTICLE: AW947
TITLE: NEW SYNTHESIS OF ALPHA-AMINO-ACIDS - AMIDOALKYLATION OF ACTIVE METHYLENE COMPOUNDS WITH GLYOXYLIC-ACID DERIVATIVES
AUTHOR: BENISHAI D (Reprint); BERLER Z; ALTMAN J
CORPORATE SOURCE: TECHNION ISRAEL INST TECHNOL, DEPT CHEM, HAIFA, ISRAEL
COUNTRY OF AUTHOR: ISRAEL
SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-CHEMICAL COMMUNICATIONS, (1975) No. 22, pp. 905-906.
ISSN: 0022-4936.
PUBLISHER: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK, MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 6
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--

L19 ANSWER 10 OF 10 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1974:118688 SCISEARCH
THE GENUINE ARTICLE: S5621
TITLE: STRUCTURAL AND CONFORMATIONAL ANALOGS OF L-METHIONINE AS INHIBITORS OF ENZYMATIC-SYNTHESIS OF S-ADENOSYL-L-METIONINE .1. SATURATED AND UNSATURATED ALIPHATIC AMINO-ACIDS
AUTHOR: COULTER A W (Reprint); LOMBARDI.JB; TALALAY P
CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT PHARMACOL & EXPTL THERAPEUTICS, BALTIMORE, MD 21205
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR PHARMACOLOGY, (1974) Vol. 10, No. 2, pp. 293-304
ISSN: 0026-895X.
PUBLISHER: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 38
ENTRY DATE: Entered STN: 1994

Last Updated on STN: 1994

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)	
GOERING H L	1948	70	3310	J AM CHEM SOC	<--

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     (FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

     FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1            43 HOMOALLYL AMINE
L2        107785 OZON?
L3             0 L1 AND L2
L4        714963 AMINO ACID
L5           433 L2(L)L4
L6       1459162 BETA
L7            82 L5 AND L6
L8        214408 ACETIC ACID
L9             5 L7 AND L8

     FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10               STRUCTURE UPLOADED
L11           47 SEARCH L10 SSS SAM
L12        13018 SEARCH L10 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13         5368 L12
L14          109 L2 AND L13
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L15           42 L2(L)L13
L16            0 L8 AND L15
L17      4884863 ACID
L18            2 L15(L)L17

     FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19           10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

     FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007

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         618058 70/RVL
           4897 3310/RPG
L20           0 GOERING H L/RAU (S) 70/RVL (S)3310/RPG

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                       9.32     358.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                       0.00      -6.24

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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       9.32     358.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -6.24

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     (FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

     FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1            43 HOMOALLYL AMINE
L2        107785 OZON?
L3             0 L1 AND L2
L4        714963 AMINO ACID
L5           433 L2(L)L4
L6       1459162 BETA
L7            82 L5 AND L6
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L8       214408 ACETIC ACID
L9            5 L7 AND L8

     FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10             STRUCTURE UPLOADED
L11            47 SEARCH L10 SSS SAM
L12         13018 SEARCH L10 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13          5368 L12
L14           109 L2 AND L13
L15            42 L2(L)L13
L16             0 L8 AND L15
L17       4884863 ACID
L18             2 L15(L)L17

     FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19            10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

     FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007
L20             0 L19

=> l2(l)l8
L21          883 L2(L)L8

=> amine
          279198 AMINE
          258623 AMINES
L22       424834 AMINE
                 (AMINE OR AMINES)
 95% OF LIMIT FOR TOTAL ANSWERS REACHED

=> l21(l)l22
L23            9 L21(L)L22

=> d l23 1-9 ti

L23  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Effects of polymer architecture and composition on the adhesion of
     poly(tetrafluoroethylene)

L23  ANSWER 2 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Process for producing low-molecular-weight polysaccharide and
     oligosaccharide thereof

L23  ANSWER 3 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Indoor air quality in museums: their existing levels, desirable conditions
     and countermeasures

L23  ANSWER 4 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of ω-functional acids

L23  ANSWER 5 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Aryl norbornane derivatives. I. Preparation of compounds

L23  ANSWER 6 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Chemistry of cyclobutanes. I. Synthesis of methylenecyclobutanes

L23  ANSWER 7 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preliminary experiments on the synthesis of colchicine: a method for the
     synthesis of ring B

L23  ANSWER 8 OF 9  CAPLUS  COPYRIGHT 2007 ACS on STN
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TI Molecular rearrangements in the hydronaphthalenic series

L23 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI β-(Hydroxyphenyl)ethylamines and their transformations. II. Synthesis of further amines and of the corresponding (hydroxyphenyl) acetic acids from natural allyl compounds

=> d l23 4 ti fbib abs

L23 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of ω-functional acids
AN 1964:82493 CAPLUS
DN 60:82493
OREF 60:14392c-e
TI Preparation of ω-functional acids
IN Naudet, Maurice; Pasero, Jean; Desnuelle, Pierre
PA Institut des Corps Gras
SO 7 pp.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1351737		19640207	FR 1963-926179	19630227
				FR	19630227

AB Fatty acids having a single point of unsatn. and also their derivs., such as esters, amides, alcohols, nitriles, amines, etc., were converted into ω-functional acids by ozonide formation at the double bond, followed by oxidation and chain splitting. The terminal function was first protected by acylation (reaction with acetic acid) before ozonolysis; the esterified reaction product was saponified or extracted as the alkali salt. In an example, 1 mole of oleyl acetate was dissolved in 750 cc. $CHCl_3$, ozonized air bubbled through to a neg. Br test, 0.5 l. H_2O added, the pH adjusted to 9, and the mixture kept 5 hrs. at 70° while 30% H_2O_2 added portionwise and alkalinity maintained. Altogether, 250 cc. H_2O_2 and 400 cc. 30° Be NaOH were used; the solvent distilled and was recovered. At the end of the oxidation, 150 cc. 36° Be, NaOH was added, the mixture refluxed 1 hr., cooled, acidified to 10% excess by 11° Be. HCl, the organic phase separated by decantation and washed to neutrality, pelargonic acid separated by steam distillation under reduced pressure, and the residue extracted with hot H_2O;
ω-hydroxy-pelargonic acid crystallized on cooling. Also prepared was ω-acetamido-pelargonic acid.

=> save temp l15 amines/a
ANSWER SET L15 HAS BEEN SAVED AS 'AMINES/A'

=> l23m and l15
             2 L23M
L24   0 L23M AND L15

=> l23 and l15
L25   0 L23 AND L15

=> logoff hold
COST IN U.S. DOLLARS   SINCE FILE ENTRY   TOTAL SESSION
FULL ESTIMATED COST   29.10   378.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)   SINCE FILE ENTRY   TOTAL

	ENTRY	SESSION
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FILE 'CAPLUS' ENTERED AT 08:46:34 ON 14 JUN 2007

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	29.10	378.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-7.02

=> help roles

CAS roles are CAS indexing terms consisting of codes that describe the new or novel information reported about a substance or a class of compounds. Specific roles have 3-letter codes. Super roles have 4-letter codes. Super roles are automatically generated from the specific roles, and are upposted for searching. Roles are available for all indexed documents from 1967 to the present.

To search a role for a specific substance, append the CAS Registry Number or a Registry File L-number answer set with a slash and the code for the role, e.g., 67-68-5/THU. To search more than one role, separate a list of roles by commas and no spaces, e.g., 67-68-5/THU,ADV. Only one role may be appended to an L-number answer set. Use the OR operator to apply multiple roles to an L-number, e.g., S L1/THU OR L1/ADV.

To search roles assigned to index headings for classes of compounds, follow the heading with a slash and the role or roles separated by commas, e.g., PHENOLS/POL,REM.

Roles are displayed in the RL (Role) field within the IT (Index Term) field. Roles are included in any display format that contains the IT or RL field. Enter SET ROLES OFF at an arrow prompt (=>) to suppress display of codes and text for roles. Enter SET ROLES CODES to display only codes. Enter SET ROLES TEXT to return to default display (codes and names). Enter HELP SET ROLES at an arrow prompt for more information.

Enter HELP THESAURUS and HELP RCODE at an arrow prompt in this file for information on using the role thesaurus to find role definitions and narrower and broader terms.

The following list contains CAS roles. Under each super role are

listed the specific roles that generate the super role.

Note that effective December 17, 2001, CAS roles were modified. The changes are summarized below and are also noted in footnotes to the list of CAS roles.

Overview of CAS role changes (effective December 17, 2001)

1. The following 4 Biological Study Roles were eliminated and replaced with more specific, newly added Biological Study roles or BSU (Biological Study, Unclassified):

   BAC Biological Activity or Effector, except Adverse
   BOC Biological Occurrence
   BPR Biological Process
   MFM Metabolic Formation

2. The following new roles were added:

   COS Cosmetic Use
   DGN Diagnostic Use
   DMA Drug Mechanism of Action
   NPO Natural Product Occurrence
   PAC Pharmacological Activity
   PKT Pharmacokinetics
   BCP Biochemical Process

   RGT Reagent

   CPN Combinatorial Preparation
   CRT Combinatorial Reactant
   CRG Combinatorial Reagent
   CST Combinatorial Study
   CUS Combinatorial Use

   CPR Chemical Process
   EPR Engineering Process
   PYP Physical Process

3. The following new super roles were added:

   RACT Reactant or Reagent
   CMBI Combinatorial Study

4. The name for NUU role was changed from Nonbiological Use, Unclassified to Other Use, Unclassified.

Note that effective December 13, 2006, CAS roles were modified as summarized below. The backfile will be updated in 2007.

Overview of CAS role changes (effective December 13, 2006

1. PNU, Preparation Unclassified role is no longer being used.

2. CPR, EPR, and PYP, introduced in 2001, are no longer being used. All will be assigned the PEP, Physical, Engineering, Chemical Process.

3. DEV, Device Component Use, is no longer being used. These will be assigned to TEM, Technical or Engineering Use.

List of CAS Roles

ANST Analytical Study

ANT Analyte
AMX Analytical Matrix
ARG Analytical Reagent Use
ARU Analytical Role, Unclassified

BIOL Biological Study

ADV Adverse Effect, Including Toxicity
AGR Agricultural Use
BAC Biological Activity or Effector, Except Adverse (1)
BCP Biochemical Process (2)
BMF Bioindustrial Manufacture
BOC Biological Occurrence
BPN Biosynthetic Preparation
BPR Biological Process (1)
BSU Biological Study, Unclassified
BUU Biological Use, Unclassified
COS Cosmetic Use (2)
DGN Diagnostic Use (2)
DMA Drug Mechanism of Action (2)
FFD Food or Feed Use
MFM Metabolic Formation
NPO Natural Product Occurrence (2)
PAC Pharmacological Activity (2)
PKT Pharmacokinetics (2)
THU Therapeutic Use

CMBI Combinatorial Study (2)

CPN Combinatorial Preparation (2)
CRT Combinatorial Reactant (2)
CRG Combinatorial Reagent (2)
CST Combinatorial Study (2)
CUS Combinatorial Use (2)

FORM Formation, Nonpreparative

FMU Formation, Unclassified
GFM Geological or Astronomical Formation
MFM Metabolic Formation (1)

OCCU Occurrence

BOC Biological Occurrence (1)
GOC Geological or Astronomical Occurrence
NPO Natural Product Occurrence (2)
OCU Occurrence, Unclassified
POL Pollutant

PREP Preparation

BMF Bioindustrial Manufacture
BPN Biosynthetic Preparation
BYP Byproduct
CPN Combinatorial Preparation (2)
IMF Industrial Manufacture

PUR Purification or Recovery
SPN Synthetic Preparation

PROC Process

BCP Biochemical Process (2)
BPR Biological Process (1)
GPR Geological or Astronomical Process
PEP Physical, Engineering, or Chemical Process
REM Removal or Disposal

RACT Reactant or Reagent (2,3)

RCT Reactant (3)
CRT Combinatorial Reactant (2)
RGT Reagent (2)
CRG Combinatorial Reagent (2)

USES Uses

AGR Agricultural Use
ARG Analytical Reagent Use
BUU Biological Use, Unclassified
CAT Catalyst Use
COS Cosmetic Use (2)
CUS Combinatorial Use (2)
DGN Diagnostic Use (2)
FFD Food or Feed Use
MOA Modifier or Additive Use
NUU Other Use, Unclassified (4)
POF Polymer in Formulation
TEM Technical or Engineered Material Use
THU Therapeutic Use

Specific roles that are not upposted to any super roles:

MSC Miscellaneous
PRP Properties

(1) Used from CA Vol. 66 (1967) to Vol. 135 (2001)
(2) Used starting with CA Vol. 136 (2002)
(3) Searching the RCT (Reactant) role retrieves references from CA Vol. 66 (1967) to the present. Searching the RACT (Reactant or Reagent) super role retrieves references with the CRT, CRG, RGT, or RCT references starting with CA Vol. 136 (2002).
(4) Starting with CA Vol. 136 (2002), the searchable text for the NUU role changed from NONBIOLOGICAL USE, UNCLASSIFIED/RL to OTHER USE, UNCLASSIFIED/RL. Search the code NUU/RL to retrieve records from CA Vol. 66 (1967) to the present.

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	30.51	379.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-7.02

FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 14 Jun 2007 VOL 146 ISS 25
FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> d his

(FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1 43 HOMOALLYL AMINE
L2 107785 OZON?
L3 0 L1 AND L2
L4 714963 AMINO ACID
L5 433 L2(L)L4
L6 1459162 BETA
L7 82 L5 AND L6
L8 214408 ACETIC ACID
L9 5 L7 AND L8

FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10 STRUCTURE UPLOADED
L11 47 SEARCH L10 SSS SAM
L12 13018 SEARCH L10 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13 5368 L12
L14 109 L2 AND L13
L15 42 L2(L)L13
L16 0 L8 AND L15
L17 4884863 ACID
L18 2 L15(L)L17

FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19 10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007
L20 0 L19
L21 883 L2(L)L8
L22 424834 AMINE
L23 9 L21(L)L22
SAVE TEMP L15 AMINES/A
L24 0 L23M AND L15
L25 0 L23 AND L15

FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

```
=> solvent\
        703417 SOLVENT
        341129 SOLVENTS
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers.  Simplify or subdivide the query and try again.  If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> solvent
        703417 SOLVENT
        341129 SOLVENTS
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
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exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> d his

     (FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

     FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1            43 HOMOALLYL AMINE
L2        107785 OZON?
L3             0 L1 AND L2
L4        714963 AMINO ACID
L5           433 L2(L)L4
L6       1459162 BETA
L7            82 L5 AND L6
L8        214408 ACETIC ACID
L9             5 L7 AND L8

     FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10               STRUCTURE UPLOADED
L11           47 SEARCH L10 SSS SAM
L12        13018 SEARCH L10 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13         5368 L12
L14          109 L2 AND L13
L15           42 L2(L)L13
L16            0 L8 AND L15
L17      4884863 ACID
L18            2 L15(L)L17

     FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19           10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

     FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007
L20            0 L19
L21          883 L2(L)L8
L22       424834 AMINE
L23            9 L21(L)L22
                 SAVE TEMP L15 AMINES/A
L24            0 L23M AND L15
L25            0 L23 AND L15
```

```
     FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

=> s solvent subset=l8
SUBSET IS IGNORED AS A SCOPE FOR THIS SEARCH
        703417 SOLVENT
<------User Break------>

=> s solvent
        703417 SOLVENT
        341129 SOLVENTS
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers.  Simplify or subdivide the query and try again.  If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> d his

     (FILE 'HOME' ENTERED AT 07:53:25 ON 14 JUN 2007)

     FILE 'CAPLUS' ENTERED AT 07:53:43 ON 14 JUN 2007
L1           43 HOMOALLYL AMINE
L2       107785 OZON?
L3            0 L1 AND L2
L4       714963 AMINO ACID
L5          433 L2(L)L4
L6      1459162 BETA
L7           82 L5 AND L6
L8       214408 ACETIC ACID
L9            5 L7 AND L8

     FILE 'REGISTRY' ENTERED AT 08:08:43 ON 14 JUN 2007
L10              STRUCTURE UPLOADED
L11           47 SEARCH L10 SSS SAM
L12        13018 SEARCH L10 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:09:50 ON 14 JUN 2007
L13         5368 L12
L14          109 L2 AND L13
L15           42 L2(L)L13
L16            0 L8 AND L15
L17      4884863 ACID
L18            2 L15(L)L17

     FILE 'SCISEARCH' ENTERED AT 08:23:44 ON 14 JUN 2007
L19           10 S GOERING H L/RAU (S) 70/RVL (S)3310/RPG

     FILE 'CAPLUS' ENTERED AT 08:27:00 ON 14 JUN 2007
L20            0 L19
L21          883 L2(L)L8
L22       424834 AMINE
L23            9 L21(L)L22
                 SAVE TEMP L15 AMINES/A
L24            0 L23M AND L15
L25            0 L23 AND L15

     FILE 'CAPLUS' ENTERED AT 08:48:09 ON 14 JUN 2007

=> allylamine or (allyl amine)
          7851 ALLYLAMINE
           675 ALLYLAMINES
```

```
          8124 ALLYLAMINE
                 (ALLYLAMINE OR ALLYLAMINES)
        106509 ALLYL
           132 ALLYLS
        106554 ALLYL
                 (ALLYL OR ALLYLS)
        279198 AMINE
        258623 AMINES
        424834 AMINE
                 (AMINE OR AMINES)
           618 ALLYL AMINE
                 (ALLYL(W)AMINE)
L26        8582 ALLYLAMINE OR (ALLYL AMINE)

=> l21 and l26
L27           2 L21 AND L26

=> d l27 1-2 ti

L27  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Effects of polymer architecture and composition on the adhesion of
     poly(tetrafluoroethylene)

L27  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Acylated Allylamines


=> d l27 s ti fbib abs
'S' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
```

SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT) containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d l27 ti fbib abs

L27 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of polymer architecture and composition on the adhesion of poly(tetrafluoroethylene)
AN 2006:623782 CAPLUS
DN 146:296544
TI Effects of polymer architecture and composition on the adhesion of poly(tetrafluoroethylene)
AU Tu, Chen-Yuan; Liu, Ying-Ling; Luo, Min-Tzu; Lee, Kueir-Rarn; Lai, Juin-Yih
CS Department of Chemical Engineering, Chung Yuan University, Taoyuan, 32023, Taiwan
SO ChemPhysChem (2006), 7(6), 1355-1360
CODEN: CPCHFT; ISSN: 1439-4235
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB Poly(glycidyl methacrylate), PGMA, chains in linear and arborescent structures were incorporated onto surfaces of poly(tetrafluoroethylene), PTFE, films by hydrogen plasma and ozone treatment and atom transfer radical polymerization The epoxide groups of the PGMA chains were further reacted with acetic acid (AAc), oxalic acid (XAc), allyl amine (AA), and ethylenediamine (EDN) to introduce hydroxyl and amine groups to the surfaces of the PTFE films. Surface characterizations performed by Fourier Transform IR attenuated total reflectance (FTIR-ATR) spectroscopy and XPS confirmed the surface modification and the chemical structure. The PGMA chains in arborescent structures show a high effectiveness for the enhancement of the adhesion of PTFE films. The adhesion of PTFE films was also significantly enhanced by ring-opening reactions of the PGMA epoxide groups with acetic acid and amine compds. A high value of 9.5 N cm-1 in the optimum 180° peel strength test was observed with PTFE/copper assemblies.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> logoff hold\
'HOLD\' IS NOT VALID HERE
For an explanation, enter "HELP LOGOFF".

=> logoff hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    14.24     394.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -0.78      -7.80

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:53:57 ON 14 JUN 2007
```